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# 3-D Matrix Ltd. (7777)

Medical technology company. Exclusively licensed from MIT, core technology is based on unique characteristics of self-assembling peptides.

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In order to highlight any biases, we clearly attribute the views. A view of the company management will always be presented as such. Our views are ours where stated. We do not try to convince or influence, only to inform.

Your suggestions and feedback are appreciated. Write to us at <u>sr_inquiries@sharedresearch.jp</u> or find us on Bloomberg.									
	FY04/07	to us at <u>sr_in</u> FY04/08	<u>quiries@snare</u> FY04/09	Gresearch.jp o FY04/10	FY04/11				
Income Statement (Million Yen)	PT 04/ 07 Par.	PT 04/ 08 Par.	Pi 04/09 Par.	Cons.	Cons.	FY04/12 Est.			
Operating Revenue	1	10	10	402	158	1,100			
YoY	-	805.2%	-4.5%		-60.6%	594.8%			
Operating Expenses	-	-	-	467	641				
YoY	-	-	-	-	37.2%				
Operating Profit	-	-	-	-65	-482	300			
YoY	-	-	-	-	637.3%	-			
OPM	-	-	-	-16.3%	-304.7%	-			
Recurring Profit	-187	-222	-259	-60	-510	256			
YoY	-	-	-	-	-	-			
RPM	-	-	-	-	-	-			
Net Income	-187	-223	-296	-61	-534	255			
YoY	-	-	-	-	-	-			
Net Margin Per Share Data	-	-	-	-	-	-			
Number of Shares (Thousands)	1,893	2,792	2,817	3,392	3,792	4,567			
EPS	-99.0	-98.5	-106.0	-19.7	-147.2	60.9			
EPS (Fully Diluted)	-99.0	-90.5	-100.0	-19.7	-14/.2	00.9			
Dividend Per Share	0.0	0.0	0.0	0.0	0.0	0.0			
Book Value Per Share	148.8	343.1	243.8	344.1	300.4	0.0			
Balance Sheet (Million Yen)	140.0	545.1	243.0	544.1	300.4				
		-	-	544	E90				
Cash and Equivalents Total Current Assets	-	-	-	594 594	589 <b>666</b>				
	-	-	-	<b>594</b> 7	6				
Tangible Fixed Assets, net	-	-	-		22				
Other Fixed Assets	-	-	-	19 579					
Intangible Assets	304	986	733	578	505				
Total Assets	504	900	/33	<b>1,198</b>	1,199				
Accounts Payable	-	-	-	12	16				
Short Term Debt	-	-	-	0	0				
Total Current Liabilities	-	-	-	31	49				
Long Term Debt	-	-	-	0	0				
Total Fixed Liabilities	-	-	-	0	0				
Total Liabilities	-	-	-	31	49				
Net Assets	282	958	687	1,167	1,150				
Interest Bearing Debt	-	-	-	0	0				
Cash Flow Statement (Million Ye	n)			20	42.4				
Operating Cash Flow	-	-	-	-28	-434				
Investment Cash Flow	-	-	-	-13	-18				
Financing Cash Flow	-	-	-	573	498				
Financial Ratios	122.207	24.691	24 504	6.201	44.001				
ROA	-123.2%	-34.6%	-34.5%	-6.3%	-44.6%				
ROE	-133.1%	-36.0%	-36.0%	-6.6%	-46.1%				
Equity Ratio	92.5%	97.1%	93.7%	97.4%	95.0%				

Source: Company Data Processed by SR Inc.

Figures may differ from company materials due to differences in rounding methods.

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### **Recent Updates**

### Highlights

SR Inc. initiates coverage of 3-D Matrix (3DM) with this report.

On **April 12**, **2012**, 3DM upwardly revised its full year FY04/12 forecasts as follows. (For original Japanese-language only release in PDF format, please <u>click here</u>.)

- Operating revenue: 1.1 billion yen (vs. previous forecast of 550 million yen)
- Operating profit: 300 million yen (vs. previous forecast of 456 million yen operating loss)
- Recurring profit: 256 million yen (vs. previous forecast of 477 million yen recurring loss)
- Net income: 255 million yen (vs. previous forecast of 478 million yen net loss)

3DM said that the upward revision of operating revenue was made due to its plan to record upfront payment revenue based on sales agreements with Fuso Pharmaceutical Industries Ltd. (TSE 4528) and Kaken Pharmaceutical Co., Ltd. (TSE 4521) regarding TDM-621 hemostatic agent for surgery (mentioned as "TDM-621" elsewhere in the report). In addition, 3DM expects to record grant revenue associated with a joint project with Japan's National Cancer Center, which also contributed to the upward revision.

3DM commented that the upward revision of operating income was due to upwardly revised operating revenue and to the steady progress in subcontracted testing and other R&D processes.

On **April 9, 2012**, 3DM announced that it reached TDM-621 domestic sales agreements with Fuso Pharma and Kaken Pharma.

(For original Japanese-language only release in PDF format, please click here.)

Based on the agreements, Fuso Pharma and Kaken Pharma will market TDM-621 in Japan.

# For corporate releases and developments more than three months old please refer to the <u>News & Topics</u> section.

Trends & Outlook						
Quarterly Performance		FY04/	12		FY04/	12
(Million Yen)	Q1	Q2	<b>Q</b> 3	Q4	% of FY	FY Est.
Operating Revenue	400	0	0	-	36.4%	1,100
YoY	-	-	-	-		
R&D Expenses	40	47	45	-		
YoY	-	-	-	-		
SG&A	150	104	112	-		
YoY	-	-	-	-		
OP	210	-151	-157	-	-	300
YoY	-	-	-	-		
OPM	52.6%	-	-	-		
RP	204	-195	-158	-	-	256
YoY	-	-	-	-		
RPM	51.1%	-	-	-		
NI	204	-196	-159	-	-	255
YoY	-	-	-	-		
NPM	51.1%	-	-	-		

Source: Company Data Processed by SR Inc.

Figures may differ from company materials due to differences in rounding methods.

**Q3 FY04/12 Results** (Announced on March 9, 2012; please refer to the preceding table.) The company maintained its FY04/12 forecast.

Q3 cumulative operating income was 400 million yen (milestone payments for the TDM-621 hemostatic agent for surgery; mentioned as "TDM-621" elsewhere in the report). Expenses stood at 498 million yen



driven by R&D costs, higher personnel costs on the back of business expansion, and IPO related costs. Consequently, the company recorded an operating loss of 98 million yen. Non-operating expenses came in at 52 million yen: 14 million yen was due to stock issuance expenses (IPO), 26 million yen in advisory costs and 7 million yen in foreign exchange losses. As a result, the company logged a recurring loss of 149 million yen and a 150 million yen net loss.

The status of 3DM's product pipeline at the end of Q3 was as follows:

### Hemostatic agent (TDM-621)

The product had been developed in Japan under the medical devices category, and in May 2011 filed an application with Japan's Pharmaceuticals and Medical Devices Agency (PMDA) for its manufacture and sale. Consequently, the company received a milestone payment tied to this development from Fuso Pharmaceutical Industries Ltd. (TSE 4528), who had been granted the exclusive right to sell TDM-621 in Japan, which drove consolidated sales for 3DM.

The company has also entered into an agreement to subcontract some of the manufacturing process for TDM-621 to Fuso Pharma, and had been working with the company to develop its system for operating as a manufacturer and vendor of this medical device.

### Alveolar bone regenerator (Development code: TDM-711)

The company has been developing this product in the US, and in July 2011 its subsidiary received IDE (Investigational Device Exemption) approval from the US Food and Drug Administration (FDA). 3DM had been holding discussions with its business partners as it prepared for the start of clinical trials, with the US clinical trials having commenced in February 2012).

### Mucous membrane protuberance material (Development code: TDM-641)

R&D for this product was ongoing. The company was negotiating with partners as it prepared for the start of clinical trials and on February 20, 2012, the company entered into an agreement with Fuso Pharma granting them an exclusive license to manufacture and sell the mucous membrane protuberance material).

### **Other Topics**

A joint Japan's National Cancer Center project proposal was selected as a "National Cancer Center Phase I Center Early Stage R&D" project, under the 2011 Ministry of Health, Labor, and Welfare's Health Labor Sciences Research Grant system. As a result, the company expected to receive a number of grants.

The company decided to establish a subsidiary in the French city of Lyon as part of its efforts to develop its business globally.

**1H FY04/12 Results** (Announced on December 9, 2011; please refer to the preceding table.) The company maintained its FY04/12 forecast.

1H revenue was 400 million yen, due to the same amount in milestone payments for the TDM-621 being booked. On the other hand, there was 341 million yen in R&D, personnel, and IPO-related expenses.. This resulted in operating profit of 59 million yen, recurring profit of 9 million yen, and net income of 9 million yen.

The company's balance sheet shows 2.5 billion yen in net assets, which was an increase of 1.4 billion yen from end-April 2011. The increase was primarily due to increases in both its capital and capital reserves of 685 million yen each, on the back of the company's IPO and the exercise of warrants. The company listed its shares on the Osaka Stock Exchange's Jasdaq Growth market on October 24, 2011 and the offering added 676 million to both its capital and capital reserves.



The status of 3DM's product pipeline was as follows:

### Hemostatic agent (TDM-621)

The company has been developing this in Japan under the medical devices category, and in May 2011 filed an application with PMDA for the manufacture and sale authorization, which was being considered by the agency. They have therefore received a milestone payment tied to this development from Fuso Pharmaceutical Industries Ltd. (TSE 4528), who had been granted the exclusive right to sell TDM-621 in Japan, which drove consolidated sales for 3DM.

The company has also entered into an agreement to subcontract some of the manufacturing process for TDM-621, and had been working with their partner to develop its system for operating as a manufacturer and vendor of this medical device.

### Alveolar bone regenerator (Development code: TDM-711)

The company was developing this product in the US, and in July 2011 its subsidiary received IDE (Investigational Device Exemption) approval from the US Food and Drug Administration (FDA). 3DM was in consultations with business partners as it prepared for the start of clinical trials.

### Q1 FY04/12 Results

Q1 business revenue was 400 million yen due to milestone payments for the TDM-621 hemostatic agent for surgery. Business expenses meanwhile came in at 190 million yen due to sales transaction fees relating to milestone payments, and increased labor costs from increased headcount. Operating income was 210 million yen; recurring profit 204 million yen; and net income was 204 million yen.

The status of the company's product pipeline was as follows:

### Hemostatic agent (TDM-621)

The company has developed this product in Japan under the medical devices category. Following the conclusion of clinical trials in FY04/11 the company filed an application in Q1 with PMDA for its manufacture and sales authorization. Given this development 3DM received a milestone payment from Fuso Pharma who owns the exclusive right to sell TDM-621 in Japan, and this drove consolidated sales for 3DM.

The company has also entered into an agreement to subcontract some of the manufacturing process for TDM-621, and had been working with their partner to develop its system for operating as a manufacturer and vendor of this medical device.

### Alveolar bone regenerator (Development code: TDM-711)

The company had been developing this product in the US, and in July 2011 its subsidiary received IDE approval from the US FDA.

### For details on previous quarterly and annual results please refer to the <u>Historical Financial</u> <u>Statements</u> section.



#### Full Year (FY04/12) Outlook

FY04/12 Forecast	FY04/11		Company	Estimates
(Million Yen)	Full-Year	1H	2H	Full-Year
Operating Revenue	158	400	700	1,100
YoY	-	-	-	594.8%
R&D Expenses	233	87		
R&D Expenses / Sales	146.9%	21.7%		
SG&A	406	254		
SG&A / Sales	256.3%	63.6%		
Operating Profit	-482	59	241	300
YoY	-	-	-	-
OPM	-	14.7%	-	-
Recurring Profit	-510	9	247	256
YoY	-	-	-	-
RPM	-	2.3%	-	-
Net Income	-534	9	246	255
YoY	-	-	-	-

Source: Company Data Processed by SR Inc.

Figures may differ from company materials due to differences in rounding methods.

Future Outlook			
Mid-Term Plan	FY04/11	FY04/12	FY
(Million Yen)	Actual	CE	
<b>Operating Revenue</b>	158	1,100	
R&D Expenses	232	-	
SG&A	406	-	

Source: Company Data Processed by SR Inc.

Figures may differ from company materials due to differences in rounding methods.

300

256

255

-482

-509

-533

On October 24, 2011, 3DM announced its mid-term plan for the period up to FY04/14. The company sees the start of domestic sales and global expansion of the hemostatic agents business as its main mission over this period. One of the important early indicators of the mission's success would be obtaining a manufacturing and marketing approval in Japan during FY04/13.

FY04/14 CF

2.977

705

892

634

634

472

1,991

401

778

453

453

452

According to the company, the revenue targets in the mid-term plan were conservative.

### FY04/13

**Operating Profit** 

**Recurring Profit** 

Net Profit

In FY04/13, the company was expecting to receive milestone payments from its distribution partners, assuming it obtains the manufacturing and marketing approval in Japan. Once the approval is acquired and the product launched, operating revenues in the form of product sales and milestone payments from sales agreements will be generated, including those from other Asian countries. As a result, the company expected to turn a profit.

### FY04/14

Operating revenues were expected to increase significantly, thanks to sales of its hemostatic agents in Japan, South Korea, and Taiwan, as well as upfront payment revenues from other contracts.

At the same time, R&D expenses were forecast to temporarily increase due to overlaps in its development pipeline (development costs were to increase as multiple clinical trials are conducted simultaneously). 3DM was planning on starting clinical trials for several pipeline applications, such as its alveolar bone reconstruction agent and hemostatic agent in the US; and its hemostatic agent in Europe. Consequently, while operating revenues were slated to increase substantially, operating profit was projected to increase only modestly.

**Development Status of Main Pipeline Applications** 

Absorbent topical hemostatic agent (TDM-621)

- Japan: the company expected to receive a manufacturing and marketing approval for Japan in FY04/13, have the product covered under the Health Insurance Portability and Accountability Act (HIP), and launch the product.
- South Korea and Taiwan: utilizing results from Japanese clinical trials, the company was aiming to acquire a manufacturing and marketing approval in these countries in FY04/13. It was hoping to bring the product to market in Korea and Taiwan in FY04/14.
- US: Preparations have been made to submit a clinical trial plan, and the company expects to start clinical trials in FY04/13 with an eye to launching the product in FY04/15.
- Europe: the company was planning to receive the CE Mark in FY04/13. (In order to sell medical devices in the EU, manufacturers must meet EU standards and the CE Mark denotes the product meets these standards.) Clinical trials were to be conducted in FY04/14 with a view to launching the product in Europe in FY04/15.

### Mucous membrane protuberance agent (TDM-641)

Japan: an application for a manufacturing and marketing approval to be filed in FY04/13 and approval is expected to be granted possibly as early as FY04/14.

### Vascular embolization agent (TDM-631)

Japan: clinical trials were planned for possibly as early as FY04/13, with an application for a manufacturing and marketing approval to be filed around FY04/14.

### Alveolar bone reconstruction agent (TDM-711)

US: clinical trials were planned for FY04/13 and FY04/14, with an application for a manufacturing and marketing approval to be filed in FY04/14.

### **Growth Projections beyond the Mid-Term Plan**

From FY04/15, 3DM expects to further accelerate growth through overseas expansion, including entry into the US market. If everything goes according to schedule, then during FY04/15 it will launch its hemostatic agent and mucous membrane protuberance agent in Japan and its hemostatic and alveolar bone reconstruction agent overseas. Based on the potential market size, SR Inc. believes European and US sales of its hemostatic agent 3DM's will become the company's main growth driver.

If however, major new pipeline products do not materialize, 3DM's R&D expenses are expected to peak out in FY04/14 and stay roughly flat going forward. , likely leading to improving profitability.



### **Mid-Term Plan Growth Projections**

FY04/12(Forecast) FY04/13(Forecast) FY04/14(Forecast) FY04/15(Forecast) FY04/16(Forecast) FY04/17(Forecast)

Source: Company Materials Processed by SR Inc.



### April 25, 2012

### Business

### **Business Description**

3DM is a medical technology company that develops, manufacturers, and markets a self-assembling peptide technology originally created at the Massachusetts Institute of Technology (MIT).

The key features of the company's business are:

- MIT holds the underlying patent for the self-assembling peptides that are the basis of the 3DM's
  products. The Company has an exclusive global license from MIT for this technology that includes rights
  of development, manufacture, and marketing of applications that use these self-assembling peptides.
- Self-assembling peptides have two main advantages over the medical products currently on the market they are intended to compete with. Firstly, as they are produced by chemical synthesis, there is no risk of viral or other types of contamination that can occur in goods derived from living organisms. Secondly, they can be mass-produced in a homogenous fashion.
- These characteristics lend themselves to potentially large-scale use in surgery (such as absorbent localized hemostatic agents and mucous membrane protuberance agents) and in the regenerative medicine field (as alveolar bone reconstruction agents).
- 3DM's business model attempts to minimize risks specific to medical product start-ups. Specifically, the
  products it is developing are categorized as 'medical devices' rather than 'pharmaceuticals'.
  Consequently, the duration from application to approval is shorter and costs are lower compared to drug
  development.

### Self-assembling peptide technology

The human body is made up of proteins, the smallest unit of which is amino acids. Peptides are molecules composed of a number of connected amino acids. Invented by Dr. Shuguang Zhang at MIT in 1992, self-assembling peptides are composed of a (16 base) RADA sequence that is made up of three types of amino acids; Arginine (R), Alanine (A), and Aspartic acid (D).

The peptides are suspended in an acidic solution, when this solution comes into contact with a neutral pH environment, for example blood or a salt solution, the peptide molecules 'self assemble' to create a gel formed of nanofibers. Once the self-assembling peptides become gelatinous, they will not revert to a liquid state even if they returned to an acidic solution. Moreover, ADME tests run on the self-assembling peptides have confirmed they do not accumulate in any particular organ, but instead degrade into protease and are excreted from the body after approximately 30 days.

The gel that is formed is an environment similar to that for cells cultured in vivo and has a network structure similar to that of an extracellular matrix, such as collagen. The company is exploiting these characteristics to create applications in a variety of fields, including surgery, regenerative medicine, and drug delivery systems (DDS).

While MIT holds the patents, 3DM has an exclusive agreement with MIT for the basic patents for the selfassembling peptide technology: PuraMatrix<sup>™</sup> is its first-generation product that uses these self-assembling peptides.

### PuraMatrix™



Source: Company Materials Processed by SR Inc.



Self-assembling peptides are non-biological molecules produced by chemical synthesis and have the following characteristics:

*Safety* – as self-assembling peptides are produced via chemical synthesis there is no risk of viral infection (as can occur in biologically-derived molecules) or contamination from foreign elements. *Homogeneity* – mass production with practically identical levels of quality is possible.

*Ease of use* – as a gel created from a solution, they are transparent and easy to handle.

*Development potential* – application potential across a wide range of fields and in development as medical devices.

### **Main Business Segments**

The Company reports only one business segment, *Medical Products*. However, this can be further broken down into the *Medical Products Development* and *Research Reagent Sales* sub-segments.

### **Medical Products Development**

In this sub-segment, the company develops medical devices and treatments for use in the fields of surgery, regenerative medicine, and DDS (drug delivery systems) based on its self-assembling peptide technology.

The main development pipeline consists of:

- Surgical field absorbent localized hemostatic agents, mucous membrane protuberance agents, and vascular embolization agents
- Regenerative medicine field alveolar bone reconstruction agents

3DM's strategy has been to develop these applications in-house as medical devices and then to obtain manufacturing and marketing approvals for them. Its sales strategy involves signing exclusive sales agreements with distributors domestically and overseas.

In the field of regenerative medicine, 3DM has been conducting research into bone reconstruction (outside of the alveolar bone space), cartilage and tendon regeneration, treatments for skin wounds, and cardiac muscle regeneration; and looking to commercialize this research.

As for the DDS space, 3DM has been working to launch products that combine self-assembling peptides with a variety of pharmaceuticals, with the peptides functioning as a carrier for the pharmaceutical agent. While it is also likely that self-assembling peptides themselves can be developed to function as pharmaceutical agents, independently developing this would be time consuming for the company. Instead it intends to license the technology out to third parties for this purpose and generate licensing revenue from doing so.

The company is also using joint research and MTA agreements with universities and other research facilities to acquire new self-assembling peptides application technologies.

### Medical Device development process

The medical products that 3DM is focused on are categorized as 'medical devices.'

The process for developing a new medical device or a pharmaceutical product follows the same sequence of basic research, preclinical trials, clinical trials, and an application for a manufacturing and marketing approval. However, with pharmaceuticals the clinical-trial stage requires a number of phases and generally speaking, involves a large number of patients. As a result, the pharmaceutical development process tends to be long.

More specifically, for pharmaceutical development the clinical trials have three phases; in Phase I and II, researchers test the drug/treatment on a small group of healthy people to evaluate its safety and effectiveness, while in Phase III they administer it to a large group of patients who suffer from the disease or condition that it is intended to treat to confirm its safety and effectiveness.

On the other hand, medical devices require a comparatively short development process of just one clinical trial phase. The R&D process for medical devices can be summarized as follows:

### Medical Device R&D Process



### R&D process for medical equipment

Source: Company Materials Processed by SR Inc.

- 1) *Basic research:* the company searches for potential medical device applications for its technologies and optimizes product specifications.
- 2) *Pre-clinical trials:* animal tests conducted to see if the product meets safety and efficacy standards.
- 3) *Clinical trials:* human trials on sufferers conducted to see if the product meets safety and efficacy standards.
- 4) *Application for a manufacturing and marketing approval:* an application is submitted to the relevant regulatory body in each country, such as the Ministry of Health, Labour and Welfare's Pharmaceuticals and Medical Devices Agency (PMDA) and the Food and Drug Administration (FDA) in the US.
- 5) *Manufacturing and marketing approval:* the relevant regulatory body issues a approval to the company.
- 6) *Inclusion in HIP/National Health Insurance schemes:* in order to be covered by Japan's national health insurance scheme (HIP) or the relevant health insurance in other countries the product's reimbursement price needs to be calculated by the authorities. In Japan, the reimbursement value will set and the product included in HIP about two to three months after the manufacturing and marketing approval is approved.
- 7) *Market launch:* the product is manufactured and goes to market.

3DM's main development pipeline consists of:

- Absorbent localized hemostatic agent (development code: TDM-621)
- Alveolar bone reconstruction agent (development code: TDM-711)
- Mucous membrane protuberance agent (development code: TDM-641)
- Vascular embolization agent (development code: TDM-631).

All of these are based on the same sequence of self-assembling peptides (RADA 16) as TDM-621. Clinical trials in humans are already underway for TDM-621 and no adverse affects were detected among the 97 patients in the trial, as of April 2012. Given this, the key point for the other products appears to be not their safety but rather their efficacy. According to the company, as long as efficacy is confirmed in clinical trials, the regulatory approval appears likely.



#### Main development pipeline

#### **Development pipeline progress**

•Development Schedule of Main Pipeline



Source: Company Materials Processed by SR Inc.

### (A) Surgical Field

3DM's main pipeline products for the surgical field are: an absorbent localized hemostatic agent, a mucous membrane protuberance agent, and a vascular embolization agent. The company also believes the there are other potentially attractive product development areas outside of the current pipeline.

### (A-1) Absorbent localized hemostatic agent (development code: TDM-621)

3DM is developing the absorbent localized hemostatic agent TDM-621 based on its RADA16 selfassembling peptide technology. TDM-621 can be applied with a syringe to comparatively narrow openings where bleeding may occur during surgery and can also be used in conjunction with an endoscope.

TDM-621 becomes pH-neutral when it comes into contact with bodily fluids, such as blood. The peptides then self assemble into nanofibers and become gelatinous. The gel perfectly coats the surface of the contact area, forming a coating that physically seals the surface film and peripheral blood vessels. In aortal blood vessels, it produces blood coagulation and hemostasis.



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# Overview of Hemostasis Application of TDM-621 Body Tissue Blood vessel Enlarged Image Blood vessel

Source: Company Materials Processed by SR Inc.

Existing hemostatic agents are categorized as liquid types (fibrin glue) or sheet/powder types (fibrin and collagen). Fibrin glue involves creating a paste out of blood-derivative fibrinogen.

There are question marks over the safety of the products currently in use as the use of blood preparation products carries the risk of infecting a patient with the hepatitis C virus. Clearly, accidental hepatitis C infections of patients have the potential to morph into a major public healthcare issue.

Blood tr	ransfusions
1987 onwards	The number of patients infected by hepatitis C virus through the use of blood products is estimated at about 10,000.
Jan 30, 2008	Reconciliation between plaintiffs and the central government following the establishment of the Act on Special Measures concerning the Payment of Benefits to Relieve the Victims of Hepatitis C Infected through Specified Fibrinogen Concentrates and Specified Coagulation Factor XI Concentrates
Dec 14, 2008	Regarding the class action lawsuits that had been brought in various areas over a period of six years, a basic agreement with the final company was executed. From this time onward, the procedures for finishing the lawsuits were taken and benefits were paid to plaintiffs.
Nov 30, 2009	The Basic Act on Hepatitis Measures was enacted (enforced in January 2010), stipulating the responsibilities of the central government to aid hepatitis patients.
Fibringl	ue
Dec 2007	First filing of an drug-induced lawsuit citing fibrin glue as the cause of infection. From this time, about 160 people brought lawsuits in various locations.
Jan 2008	The Act on Special Measures concerning the Payment of Benefits to Relieve the Victims of Hepatitis C Infected

through Specified Fibrinogen Concentrates and Specified Coagulation Factor XI Concentrates was enacted (fibrin glue was also targeted). March 2009 The central government, which had put reconciliation procedures on hold, announced a policy of proactive

March 2009 The central government, which had put reconciliation procedures on hold, announced a policy of proactive reconciliation.

Source: Company Materials Processed by SR Inc.

TDM-621 has a number of advantages over existing hemostatic agents. First, there is no risk of infection. The majority of hemostatic agents currently in use are synthesized from human or animal blood, such as from fibrinogens, while the raw material for collagen is produced from the skin of animals. As these products are derived from living organisms, they carry the risk of viral infection. In contrast, TDM-621 is chemically synthesized from amino acids and so carries no risk of viral infection or contamination from unknown elements.

The medical use of biologically derived products is subject to strict controls:

- Informed consent. Patients (or their families) must receive an appropriate explanation about their use and risks
- Records of production and use must be kept
- Reports must be created verifying absence of infectious diseases in the products

As TDM-621 is chemically synthesized product, there is no infection risk. Apart from obvious healthcare and legal benefits, this could also reduce administrative burden. In cases when biologically derived hemostatic agents are used, patients (or their representatives) must sign off a consent form before the

start of the surgery. When TDM-621 is used, no consent is required. Infections transmitted during medical procedures have emerged as a serious public health issue in the recent years and there is substantial latent demand for new medical agents that can eliminate the risk of infection, reduce surgery time and alleviate the burden on patients.

From a surgeon's perspective, TDM-621 also has a number of appealing features. A transparent liquid, it becomes pH-neutral gel only after coming into contact with bodily fluids such as blood. Therefore, it does not obscure a surgeon's view and can be easily applied via a catheter or into a narrow tissue entrance. In contrast, standard hemostatic agents are cloudy liquids and can obscure a surgeon's view of a damaged area, especially when operating remotely with a camera. Finally, unlike surgical glue, TDM-621 does not self-solidify, so it can be applied via a catheter.

3DM notes that TDM-621 induces hemostasis in, and perfectly seals surface membranes and peripheral blood vessels, meaning it can induce a greater hemostatic effect than existing products (which induce hemostasis by bonding the tissue or covering it with an adhesive agent.

### Image of DM-621



Source: Company Materials Processed by SR Inc.

TDM-621 is dispensed as a prefilled syringe product adding to ease of use. Any residual left in the body breaks down into amino acids and is naturally excreted over the course of several days.

To eliminate the risk of administering potentially dangerous dosages, 3DM has introduced a number of measures to prevent accidental dangerous use. For instance, TDM-621 is prefilled in a syringe with a non-standard tip that prevents attaching needles and limits the amount of substance to recommended levels (see image above).



• Shared Research •

### **TDM-621** Features

	TDM-621	Liquid Type (Fibrin Glue)	Sheet/Powder Type (Fibrin & Collagen)
Raw Material (Infection Risk)	Chemically Synthesized (no infection risk)	Derived from humans and cows (infection risk present)	Derived from humans and animals (infection risk present)
Informed Consent	Not required	Required	Required
Ease of Use (Preparation, Application, Lead Time etc.)	Immediately usable	Requires mixing before use	Immediately usable, but requires compression
Margin for Error and reapplication of treatment	Possible	Not Possible	Not Possible
Compatibility with surgeon's field of vision	Transparent liquid	Transparent white liquid	White, non-transparent
Hemostatic effect	Hemostasis via closure of blood vessels and forming a surface film	Hemostasis by adhesion	Hemostasis as an adhesive cover
Broader Applications	Endoscope & laparoscope use	None	None
Post-surgical removal process	Dissolvable in saline solution	Difficult	Difficult

Source: Company Materials Processed by SR Inc.

### TDM-621 R&D Status

3DM launched clinical trials in January 2010 for TDM-621 in order to apply for a Japanese manufacturing and marketing approval. 97 clinical trial patients were chosen who exhibited the following symptoms:

- Exudative (oozing) hemorrhaging from wounds in coronary artery bypass surgery and artificial vascular replacement surgery
- Exudative hemorrhaging from the wound surface in hepatic resection surgery
- Exudative hemorrhaging from the mucosal resection part or submucosal layer during upper gastrointestinal tract endoscopic mucosal resection surgery, and endoscopic submucosal dissection.

Clinical trials were completed in April 2011.

TDM-621's hemostatic efficacy has been generally confirmed in clinical trials and tests five to seven days after surgery did not detect any problems. The product also received high praise by the doctors conducting the Japanese clinical trials. Based off the clinical-trial results, the company submitted a manufacturing and marketing approval application in May 2011 to the PMDA for TDM-621. If the process goes smoothly, as of April 2012, the product was expected to receive approval by mid-2012, and launched in Japan sometime later in 2012.

Plans were also afoot to commercialize and market TDM-621 in Asia ex-Japan. On September 17, 2011, 3DM concluded a partnership agreement with Daewoong Pharmaceutical Co. of South Korea and a licensing agreement with Excelsior Medical Co. of Taiwan. Japanese pre-clinical and clinical trial data confirming the safety and effectiveness of TDM-621 was slated for use for the South Korean and Taiwanese regulatory approval processes (i.e. the company was to conduct bridging studies).

If these bridging studies are recognized as valid by the authorities in these two nations, then the 3DM can be expected to acquire a manufacturing and marketing approval for both countries in a comparatively short period of time. However, if the bridging studies are not recognized, it will have to carry out additional South Korean and Taiwanese clinical trials.

In the US, the company was planning on preparing and submitting a clinical trial plan in 2012, with an eye

to starting clinical trials in FY04/13. As of April 2012, it was aiming for a US product launch during FY04/15.

In Europe, the plan was to use the company's French subsidiary to acquire a CE Mark in FY04/13. (CE Marks are required certification for selling medical devices in the EU and denote EU safety standards have been met.) While 3DM will be able to sell TDM-621 once it receives its CE Mark, it will need to conduct clinical trials if it wishes the product to be covered by national health insurance schemes in Europe. Therefore, as of April 2012, it was conducting European clinical trials with the goal of being covered under the health insurance schemes of the main European countries by FY04/15.

### TDM-621 Sales Agreements

In May 2011, 3DM concluded an exclusive sales agreement for TDM-621 in Japan with Fuso Pharmaceutical Industries Ltd. (TSE 4538). The company has already received an upfront payment and a milestone payment (triggered by the confirmation of the regulatory approval application). It will receive a further undisclosed milestone payment upon receiving the manufacturing and marketing approval for TDM-621. Furthermore, Fuso Pharmaceutical is obliged to purchase a minimum volume of TDM-621 from 3DM for approximately 10 years.

Fuso Pharmaceutical was chosen as a partner as it recognized the value and potential of the product from an early stage.

As previously mentioned, 3DM has also concluded agreements with Daewoong Pharmaceutical of South Korea and Excelsior Medical of Taiwan. Daewoong Pharmaceutical is one of South Korea's leading pharmaceutical companies, and Excelsior Medical one of Taiwan's top medical devices manufacturers.

Assuming the same pricing as for existing hemostatic products, SR Inc. anticipates a sales price of around 14,000 yen/1cc. However, when considering the competitive advantages of TDM-621, it is conceivable that a premium could be charged.

### (A-2) Mucous membrane protuberance agent (development code: TDM-641)

R&D for 3DM's self-assembling peptide based agent that is injected into the mucous membrane during endoscopic procedures to form a protuberance on the tumor site is ongoing. TDM-641 is intended for use in endoscopic surgery for stomach cancer, endoscopic mucosal resection (EMR) surgery and endoscopic submucosal dissection (ESD) surgery for esophageal cancer.

The company is developing TDM-641 as an agent to be injected into the submucosal layer in endoscopic procedures and causes the affected area to protrude. Based on the product's feature – namely, of forming a pH neutral gel on coming into contact with a liquid, such as blood – it has been confirmed in animal experiments that not only can TDM-641 produced the protuberance, but that it also possesses a secondary hemostatic effect. Naturally, saline and sodium hyaluronate do not provide this hemostatic effect and it is hoped that TDM-641 will reduce the difficulty of these operations.



#### Overview of the mucous membrane protuberance method



Source: Company Materials Processed by SR Inc.

#### TDM-641 R&D Status

Both TDM-641 and TDM-621 use the same RADA 16 self-assembling peptides as their raw material, although the concentration of the peptides varies for the two. Consequently, safety data obtained in clinical trials for TDM-621 can also be used for TDM-641. As of April 2012, 3DM was preparing additional clinical trials required to confirm the safety of TDM-641.

#### TDM-641 Sales Agreements

In February 2012, the company signed an exclusive sales agreement for TDM-641 in Japan with Fuso Pharmaceutical Industries.

### (A-3) Vascular embolization agents (development code: TDM-631)

3DM has been pursuing R&D of its RADA 16 self-assembly peptides technology for use as an intravascular embolization agent in hepatic artery embolization surgery and uterine artery embolization surgery, the development code for this product is TDM-631.

In hepatic artery and uterine artery embolization surgery, TDM-631 is injected via a catheter into the embolus in the artery, this blocks the artery that provides the liver or uterine tumor with nourishment and by cutting off the blood supply the tumor dies. As TDM-631 becomes gelatinous when it comes into contact with a liquid, it can be injected into the artery via a catheter and used to close the intravascular cavity the company is exploring TDM-631's use as a new type of embolization agent.

### TDM-631 R&D Status

In pre-clinical trials, 3DM confirmed TDM-631 becomes gelatinous within an intravascular cavity after it was dissolved in a contrast agent and had been injected into the cavity via a catheter. Moreover, it confirmed that the gelatinous TDM-631 can be checked visually using an X-ray camera. Going forward, once the company's mucous membrane protuberance agent enters the clinical development stage, 3DM plans to conduct testing towards the clinical development of its vascular embolization agent.



### **Embolization Therapy**





Embolization of cerebral aneuryms

Source: Company Materials Processed by SR Inc.

### (B) Regenerative Medicine

Self-assembling peptides have a physical structure similar to an extracellular matrix that supports cell reproduction. As a result, 3DM has been looking to apply its technology to the field of regenerative medicine and one of its pipeline products is an alveolar bone reconstruction agent. The company is eying a US commercial launch for dental implant use.

Outside of its immediate product pipeline, 3DM has also been conducting research on self-assemblingpeptide technology's use in bone reconstruction other than alveolar bone surgery; its application in cartilage and tendon regeneration; skin wound treatment; and regeneration of cardiac muscles. In particular, the company believes its technology has significant potential for skin-wound treatment.

### (B-1) Alveolar bone reconstruction material (development code: TDM-711)

Alveolar bone degradation due to periodontitis can cause teeth to drop out. In such cases, a artificial teeth can be artificially implanted, however, if there is not enough bone to affix the artificial teeth to then alveolar bone reconstruction surgery is required beforehand. 3DM has been developing TDM-711 as a scaffolding material for alveolar bone reconstruction bone reconstruction.

The nanofibers created by self-assembling peptides in their gelatinous form have a structure similar to the biological environment required for cells proliferation. By filling in areas where there is a lack of bone, TDM-711's characteristics allow it to function as a scaffolding material to promote bone reconstruction.



Source: Company Materials Processed by SR Inc.



Not many surgeons in the US use bone substitute material when conducting alveolar bone reconstruction surgery as part of implant treatment. Instead the patient's own bone, a bone allograft, or artificial bone is favored. 3DM is investigating the use of TDM-711 to improve bone take-up in reconstruction procedures that use bone allograft or artificial bone. Additionally, TDM-711 carries no risk of infection and should improve patients' quality of life.

### TDM-711 R&D Status

The company performed GLP-compliant confirmatory tests of the efficacy of TDM-711 on patients with alveolar bone defects. As significant bone regeneration was confirmed compared to the control group, the company then continued R&D of TDM-711 and submitted an IDE approval application to the FDA in September 2010. The approval was granted in July 2011. In February 2012, it commenced clinical studies at the Forsyth Institute (an independent non-profit research center affiliated with Harvard University).

### (C) DDS Field

3DM has been researching the possibility of using self-assembling peptides as a carrier in drug delivery systems (DDS). It has also conducted multiple efficacy trials into the controlled release of proteins, including bFGF and PDGF. The surfactant peptide A6K is drawing particular attention. A characteristic of A6K is that it forms nanotubes in liquids. 3DM is researching whether this characteristic can be used to deliver siRNA encased inside nanotubes through the cell membrane and inside cancer cells.

### DDS R&D Status

3DM is conducting joint research with the National Cancer Center in pursuit of new cancer therapy technologies using surfactant peptides and has commenced basic research focusing on controlled release targeting cancer cells.

In the surgical and regenerative medicine fields, the company is able to independently carry out clinical trials and acquiring manufacturing and marketing approvals. But in the DDS field, product development focuses on the commercialization of its research products as pharmaceutical drugs. Here 3DM strategy is to license its technology to major pharmaceutical companies.

### **Medical Reagent Sales**

The self-assembling peptides product, PuraMatrix<sup>™</sup>, is sold by Becton, Dickinson and Company as a research reagent to universities and other research facilities around the world. PuraMatrix<sup>™</sup> is used in a variety of medical applied studies and 3DM is marketing the product as a research reagent in the hope that the researchers using will develop new commercially viable applications.

### Main business partners

The company is outsourcing the manufacture of the peptide raw materials to CPC Scientific Inc. (unlisted) and two other companies, all of which appear to supply exclusively to 3DM.

### Absorbent localized hemostatic agent (TDM-621)

In May 2011, 3DM signed a manufacturing outsourcing agreement with Fuso Pharmaceutical Industries Ltd. and part of manufacturing process (pre-filling of syringes) has been exclusively outsourced to Fuso.

In April 2009, 3DM concluded a business tie-up agreement with Itochu Chemical Frontier Corporation (subsidiary of Itochu Corp. (TSE 8001)), for it to carry out raw peptide material procurement, outsourcing of manufacturing, and sales on for 3DM. A cooperation and support system was also implemented.

The company has an exclusive sales agreement with Fuso Pharmaceutical for distribution in the Japanese market. It has also signed exclusive agreements with Daewoong Pharmaceutical Co. of South Korea and Excelsior Medical Co. of Taiwan for sales in these two countries.

### Mucous membrane protuberance agent (TDM-641)

The company has an exclusive sales agreement with Fuso Pharmaceutical for sales and distribution in Japan.

### **R&D System**

3DM's R&D activities are carried out by two departments:

- Pharmaceutical Development Department (three staff) handling manufacturing and marketing approval applications and quality control systems
- Business Development Department (six staff) handling the sourcing of clinical-trial facilities, doctors for the trials, and the clinical monitoring required.

The company has also signed self-assembling peptide technology MTA agreements with over 100 universities and research institutes worldwide. 3DM has been conducting joint research with these partners with an eye to developing new applications for its technology. In these joint-research agreements, the personnel and funds are sourced from its partners, while the company is left to acquire the rights to commercialize any results.

### **Relationship with MIT**

MIT holds the substance patent and the method-of-use usage patent for the self-assembling peptides (collectively termed "the basic patents"). (The current US subsidiary) 3DM, Inc. concluded an exclusive patent license agreement with MIT in April 2003 for the worldwide license (including re-licensing rights) to its patents in the fields of medicine, life sciences, and beauty care. In October 2004, 3DM, then a Japanese subsidiary, signed a license-and-supply agreement with 3DM, Inc. and acquired the patent rights for Asia. In October 2007, the contract was revised following 3DM becoming the parent of 3DM, Inc.

The basic patents cover all the peptides that self assemble to form a hydro-gel, and while there are some variations across regions, the main patents have all been registered.

A list of both self-developed patents awaiting approval and those that the company acquired through its exclusive license deal with MIT follows:



### April 25, 2012

Product Pipeline	Patent Description	Patent No	Territory	Patent Holder	Registration Date Date	Expiry Date
Substance Patent						
Absorbable	Self-Assembly Peptide Substance Patent	US 5670483	US	MIT	September 23, 1997	November 29, 2014
	Self-Assembly Peptide Substance Patent (self- assmebly and inhibition	US 6548630	US	MIT	April 15, 2003	July 21, 2017
	Self-Assembly Peptide Substance Patent	WO 06/014570	US (Patent pending)	Subsidiary	-	-
Patent Applications		1		1		
Absorbable local hemostatic material Prominence material mucosa	Self-Assembly Peptide Hemostatic agent and methods for blocking assembly	2008-259860	Japan (Patent pending)	3-D Matrix	-	-
Alveolar bone reconstruction material PuraMatrix	Self-Assembly Peptide Cell Culture Method	US 5955343	US	MIT	September 21, 1999	August 21, 2014
Alveolar bone reconstruction material PuraMatrix	Self-Assembly Peptide Cell Culture Method	US 6800481	US	MIT	October 5, 2004	March 25, 2017
PuraMatrix DDS	Self-Assembly Peptide Protein DDS	US 7098028	US	MIT	August 29, 2006	March 16, 2023
DMathái	Self-Assembly Peptide	US 7449180	US	MIT	November 30, 2008	February 5, 2021
PuraMatrix	Cartilage Cell Culture Method	EP 717398	EU	MIT	December 31, 2008	February 5, 2022
PuraMatrix	Self-Assembly Peptide Modified peptide Substance Patent	US 7713923	US	MIT	May 11, 2010	June 24, 2024
PuraMatrix	Self-Assembly Peptide Nerve Regeneration Method	US2005/0287186	US	MIT	-	-

Note: Modified self-assembly peptide patents have been filed internationally in the EU, Japan, and Canada under the Patent Cooperation Treaty (PCT) and currently under review

Source: Company Data Processed by SR Inc.

Contract company	Subsidiary (3-D Matrix Inc.)
Counterparty	MIT
Contract Title	<ul> <li>「AMENDED AND RESTATED EXCLUSIVE PATENT LICENSE AGREEMENT」</li> <li>「FIRST AMENDMENT」、「SECOND AMENDMENT」,「THIRD AMENDMENT TO AMENDED AND RESTATED EXCLUSIVE PATENT LICENSE AGREEMENT」</li> </ul>
Contract period	Basic patents covered until patent expiry, others covered until expiry or patent application abandoned
Main Agreement	Licensing MIT grants 3-D Matrix Inc. exclusive global licensing rights (incl. sub-licensing rights) of self-assembling peptide patents owned by MIT as well as those for

Source: Company Data Processed by SR Inc.

Among the basic patents, the first one expires in 2014 and others begin to expire thereafter. However, even as the first patent expires, 3DM believes managing its patents as a portfolio should continue to form a barrier to entry and thus it will be able to maintain its competitive advantage. It is working on its patent strategy with a prominent law firm based in Boston (Choate Hall & Stewart LLP).

A number of Bain & Co. alumni, including the current chairman of 3DM Keiji Nagano, co-invested as angel investors when 3DM, Inc. was formed and exclusive commercialization rights to self-assembling peptides technology were acquired from a group of MIT researchers in May 2001.

#### **Group Companies**

- 3DM, Inc.: a 100% owned subsidiary based in Massachusetts, US.
- 3DM Europe SAS.: a 100% owned subsidiary based in Lyon, France.

### **Business Model**

3DM's business model is significantly different to that of conventional drug discovery start-ups. One of the



things that made this possible is a unique nature of self-assembling peptides.

### **Medical Device Business Flow-Chart**



Source: Company Materials Processed by SR Inc.

The diagram above shows the business flow for 3DM's Medical Products segment.

Company revenues can be categorized into 1) upfront payments, 2) milestone payments, and 3) revenues from product sales. Upfront payments are received from licensee pharmaceutical companies when the agreement is signed, while milestone payments are generated in the development process when certain goals are achieved. This is the same as with conventional drug-discovery venture companies. The major difference is that in the case of 3DM, the company develops the substance as a medical device itself and independently seeks a manufacturing and marketing approval. Therefore, if its products reach the market, 3DM will sell them directly to pharmaceutical companies at a certain percentage of the final market price. What this means is that 3DM gets a substantially larger portion of the sales revenues compared to conventional drug discovery startups.

What makes this possible is the fact that peptide-based substances that 3DM is developing are "medical devices" as opposed to "drugs". This means substantially shorter and less expensive path to the regulatory approval. For instance, the company began developing its absorbent localized hemostatic agent (TDM-621) in Japan around 2009 and if it brings TDM-621 to the market during FY04/13 as planned, it will mean it took 3-4 years from scratch to launch. Furthermore, 3DM claims it can keep development costs down by actively using outside parties. Also, all 3DM pipeline products use basically the same raw material (the RADA 16 self-assembling peptides). Therefore, once it successfully completes clinical trials for the first product, it should be able to shorten the time to market for the subsequent products.

In FY04/12, the majority of 3DM's revenues are expected to come from upfront and milestone payments. However, from FY04/13 on, if the launch of TDM-621 and other products goes according to schedule, product sales revenues will also be recorded. The company anticipates that the weight of such revenues will grow in the future, leading to greater and more stable profits.

The gross profit margin is 100% for upfront and milestone payments. For product sale revenues the company expects the GPM of around 60% at the start around 70% once the mass production scale effect



kicks in.

Because 3DM has acquired the exclusive rights to the patents from MIT, it pays a license fee to MIT as a fixed percentage of sales. However, SR Inc. anticipates that this license fee will not exceed few percentage points.

3DM pays a fee for the outsourced peptide raw materials. In addition, it pays certain advisory and assistance fees to such parties as CROs and pharmaceutical consultants.



### Overview of the company's business model



As 3DM deals with medical devices there is a standardized manufacturing process for its products and the risk of bottlenecks in raw material procurement, manufacturing, or at other points in the supply chain is low.



### Strengths & Weaknesses Strengths

- Promise of the core self-assembling peptide technology: self-assembling peptides have a number of advantages compared to their biocompatible material rivals, including safety and ease of use. Moreover, the material can be used across a wide field of applications. 3DM has been granted the exclusive worldwide license (including re-licensing rights) from MIT for the basic patents. Consequently, barriers to entry for competitors appear to be high, both in terms of technology and intellectual property rights.
- Differentiated business model: the company is focused on the development of medical devices, which means the product development period needed is relatively short when compared to the time it takes to develop standard drugs. Moreover, development costs are also lower for medical devices than drugs. Finally, 3DM relies on third parties for development of its medical products helping minimize its own employee numbers.
- Large potential market: 3DM's target markets of hemostatic agents and alveolar bone reconstruction agents are both expected to grow in the future. SR Inc. believes the superiority of its core technology and its exposure to growth medical markets puts the company in a sweet spot.

### Weaknesses

- Commercial success depends on outside partners: given the company has chosen to focus on searching for pipeline products, accumulating medical device development expertise, and specializing in 'project management and business strategy', choosing the right partners for its other functions is critical to the company's success.
- Dependence on third party core patents with relatively short lives: one potential weakness for the company is the fact that most of the patents that form the core of 3DM's technology are licensed (albeit exclusively) from MIT and are due to expire in the period between 2014 and 2024. 3DM is aware of potential challenges and counters that clever intellectual property management strategy would sufficiently ensure legal control of the related technologies. In fact, the company has retained a prominent law firm to advise it on the patent strategy.
- Potential human resources bottlenecks: the majority 3-D Matrix's functions are dependent on third parties, which helps ameliorates human resource bottlenecks as the company grows. However, the company must still secure personnel with the necessary levels of expertise in order to carry out the project functions it has chosen to focus on. Consequently, it still faces some human resource hurdles in its efforts to grow its business.



### Market and Value Chain Japan's hemostatic agent market



Source: Company Materials Processed by SR Inc.

### Overview of the hemostatic agent market

Hemostatic agents are used in surgery in areas such as cardiac and vascular, respiratory, digestive, and neurosurgery. The Japanese market is estimated to be worth approximately 17 billion yen. The Yano Economic Research Institute has forecast the market will remain more or less at this scale going forwards. However, most of the currently used products are fibrin glue-type or collagen-type, both of which use materials derived from living organisms and so carry the risk of infection from viruses that may reside within these materials. A string of companies have been forced to withdraw from the market as they have been unable to meet heightened safety standards following revisions to the Pharmaceuticals Affairs Law. This and other factors have led to market stagnation.

After TDM-621 is launched, the Company is aiming to capture 50% market share based off TDM-621 replacing existing products on the market. The company is also expecting the domestic market to grow to around 30 billion yen. The biggest reason is that currently surgeons are refraining from using hemostats due to concerns about the risks associated with animal/human origin of the existing products. TDM-621 resolves this problem and should trigger more liberal use. The company also develops new end applications such as use in combination with an endoscope or peritoneoscope.

Hemostatic agents are widely used during surgery in the US. Due to the increasing number of operations driven by an aging society, the American hemostatic agent market is expected to grow at an annual average rate of 6% and be worth 1.3 billion dollars by 2016, according to iDATA Research. The European market is also forecast to reach a similar size. 3DM believes it can capture a 30-50% share of both the European and US markets.



#### **Forecast Trends for US Hemostatic Market**



Source: Company Materials Processed by SR Inc.

### Overview of the mucous membrane protuberance agent market

Around 800,000 endoscopic lesion resections are performed annually in Japan and this number is increasing by about 10% per annum, according to a survey by the Ministry of Health, Labour and Welfare.

### Overview of the vascular embolization agent market

There were 113,685 head, thorax, and abdominal surgical procedures and 11,526 procedures using anticancer agents in arterial embolization to treat uterine myoma performed in Japan, according to a Ministry of Health, Labour and Welfare survey.

### Overview of the alveolar bone regeneration agent market

About 600,000 implant procedures are carried out in Japan each year. However, in the US about 10 times this number is performed. Moreover, alveolar bone reconstruction surgery in the US is expected to grow annually by 5.6% out to 2014, according to the Millennium Research Group.



Source: Company Materials Processed by SR Inc.



### April 25, 2012

### **Barriers to Entry**

3DM's core self-assembling peptide technology produces agents that have a number of advantages compared to other biocompatible materials, including safety and ease of use. The company has also obtained from MIT the exclusive global rights (including re-licensing rights) for the basic patents for this technology. Consequently, from both a technological and intellectual-property-rights perspective barriers to entry are extremely high.

### Competition

According to MedMarket Diligence, in 2009 the global market for hemostats was dominated by major corporations such as CSL Behring (Unlisted), Johnson & Johnson (JNJ US), King Pharmaceuticals, Inc. (Unlisted; Pfizer Inc. subsidiary), Nycomed (Unlisted; Takeda Pharmaceuticals subsidiary), and Baxter International Inc. (NYSE, BAX). Pfizer Inc. (NYSE, PFE), HemCon Medical Technologies, Inc. (Unlisted) and Integra Lifesciences Corp (NASDAQ, IART) were also prominent.

The main hemostatic agents in the Japanese market include:

- Bolheal, a fibrinogen preparation. The product is manufactured by the Chemo-Sero-Therapeutic Research Institute (Kaketsuken) and distributed by Astellas Pharma Inc. (TSE, 4503) and Teijin Pharma Ltd., a subsidiary of Teijin Ltd. (TSE 3401)
- Tachocomb, manufactured by CSL Behring
- Abiten, a collagen-type absorbent localized hemostatic agent, manufactured by Zeria Pharmaceutical Co. (TSE 4559).
- Arista AH, an absorbent localized hemostatic agent, developed by Medafor, Inc. and distributed by Mera Pharmaceuticals Inc.

It appears that 3DM's products are superior, particularly in terms of safety. Of many products available in the market, Medafor's Arista AH is derived from starch rather than from living organisms but 3DM feels that its product is sufficiently superior.



### Strategy

3DM strategy is to develop and commercialize products across a variety of fields based on its selfassembling peptide technology, using outside partners to supply it with manufacturing and distribution capabilities while it focuses on developing the pipeline, accumulates medical device development expertise, and recommends commercialization strategies.

If the company can build a strong distributor network and find partners able to aggressively market its products, then the products appear to be likely to realize their potential and capture significant market share. On the other hand, if its distributor network is weak or it ends up partnering with companies who feel that the company's products are a threat to their existing product line-up then 3DM's products are unlikely gain much traction.

3DM has believes the strength of its products provides it with a strong negotiating position when dealing with current or potential partners. As of April 2012, it was working with an outside consulting company to refine its distributor strategy in areas such as pricing, including for after a product has been included in national health insurance systems, and for the selection of business partners.



## **Historical Financial Statements**

### Income Statement

Income Statement						
Income Statement	FY04/07	FY04/08	FY04/09	FY04/10	FY04/11	FY04/12
(Million Yen)	Par.	Par.	Par.	Cons.	Cons.	Est.
Operating Revenue	1	10	10	402	158	1,100
YoY	-	805.2%	-4.5%	-	-60.6%	594.8%
CoGS	-	-	-	1	2	
R&D Expenses	-	-	-	111	233	
SG&A	-	-	-	355	406	
Total Business Expenses	-	-	-	467	641	
Operating Profit	-	-	-	-65	-482	300
YoY	-	-	-	-	-	-
OPM	-	-	-	-	-	-
Non-Operating Income	-	-	-	11	0	
Non-Operating Expenses	-	-	-	5	27	
Recurring Profit	-187	-222	-259	-60	-510	256
YoY	-	-	-	-	-	-
RPM	-	-	-	-	-	-
Extraordinary Gains	-	-	-	-	-	
Extraordinary Losses	-	-	-	-	3	
Tax Charges	-	-	-	1	21	
Net Income	-187	-223	-296	-61	-534	255
YoY	-	-	-	-	-	-
Net Margin	-	-	-	-	-	-

Source: Company Data Processed by SR Inc.

Figures may differ from company materials due to differences in rounding methods.

### FY04/11

Total sales were 158 million yen (vs. 402 million yen in FY04/10), driven by 150 million yen in upfront payments (vs. 400 million yen in FY04/10). Operating expenses meanwhile came to 641 million yen, an increase of 174 million yen from FY04/10. This was mainly due to a 50 million yen increase in SG&A expenses from increased headcount, and a 122 million yen rise in R&D expenses from higher clinical trial expenses for TDM-621. This resulted in an operating loss of 482 million yen (vs. 65 million yen in FY04/10); a recurring loss of 510 million yen (vs. 60 million yen in FY04/10), and a net loss of 534 million yen (vs. 61 million yen in FY04/10). The status of the company's product pipeline was as follows:

### Hemostatic agent for surgery (TDM-621)

Clinical trials began in FY04/10 and ended in FY041/11. The company then filed an application with PMDA for the manufacturing and sales authorization in FY04/11. In August 2010 the company received authorization for Type One medical devices manufacture and sale.

In September 2010, the company entered into a partnership agreement with Daewoong Pharmaceutical Co. (Korea A069620), granting them exclusive rights for sales in Korea; it also signed a licensing agreement with Excelsior Medical Co. (Taiwan 4104), granting it exclusive rights to develop, manufacture, and sell the product in Taiwan. Upfront payments from both companies contributed to sales at 3DM.

### Alveolar bone regenerator (Development code: TDM-711)

The company had been developing this product in the US, and in March 2011 its subsidiary received conditional Investigational Device Exemption (IDE) approval from the US Food and Drug Administration (FDA). Of the three possible responses to an IDE application (Approval, Approval with changes, Not Approved), this conditional approval corresponded to "Approval with changes".



#### **Balance Sheet**

Balance Sheet	FY04/07	FY04/08	FY04/09	FY04/10	FY04/11
(Million yen)	Par.	Par.	Par.	Cons.	Cons.
ASSETS					
Cash and Equivalents	-	-	-	544	589
Inventories	-	-	-	33	39
Other Current Assets	-	-	-	17	39
Total Current Assets	-	-	-	594	666
Total Tangible Fixed Assets	-	-	-	7	6
Total Other Fixed Assets	-	-	-	19	22
Goodwill	-	-	-	537	467
Patents	-	-	-	42	38
Total Intangible Assets	-	-	-	578	505
Total Fixed Assets	-	-	-	604	533
Total Assets	304	986	733	1,198	1,199
LIABILITIES					
Accounts Payable	-	-	-	12	16
Accrued Expenses	-	-	-		
Short Term Debt	-	-	-	0	0
Other Current Liabilities	-	-	-	15	9
Total Current Liabilities	-	-	-	31	49
Long Term Debt	-	-	-	0	0
Other Fixed Liabilities	-	-	-	0	0
Total Long Term Liabilities	-	-	-	0	0
Total Interest Bearing Debt	-	-	-	0	0
Total Liabilities	-	-	-	31	49
SHAREHOLDER EQUITY (NET ASSETS)	-	-	-		
Issued Capital	-	-	-	1,109	1,359
Reserves	-	-	-	1,099	1,349
Retained Earnings	-	-	-	-1,063	-1,596
	0	0	0	0	11
Total Shareholder Equity (Net Assets	282	958	687	1,167	1,150
Working Capital	-	-	-	21	22
Interest Bearing Debt	-	-	-	0	0
Net Debt	-	-	-	-544	-589

Source: Company Data Processed by SR Inc.

Figures may differ from company materials due to differences in rounding methods.

#### Assets

The company assets are mostly cash and equivalents, as well as goodwill (resulting from the acquisition of its former US parent; amortizing at about 70 million yen p.a. through FY04/19).

### Liabilities

The company is debt free as of the end of FY04/11.

#### **Net Assets**

As a pharma startup, 3-Matrix has to incur R&D costs even before its products hit the market and as a result has negative retained earnings as of the end of FY04/11.

The company has also conducted the following capital increases, primarily through issuance of new equity:

- October 2007: Third-party share allocation of 579 million yen (1,448 common shares issued to 3DM Investment LLC., and Massachusetts Institute of Technology)
- November 2009: 500 million yen third-party allocation (1,250 common shares issued to Yasuda Enterprise Development Co. No. 4 Business Investment Limited Partnership; JAIC SME Global Support Investment Limited Partnership; So-net M3 Inc. (now M3 Inc.); Jafco Sangaku Bioincubation Investment Business Limited Partnership; and TAIB-JAIC Asian Balanced Private Equity Fund)
- September 2010: 200 million yen third-party allocation (400 common shares issued to Fuso Pharmaceutical Industries Ltd.)



- September 2010: 300 million yen third-party allocation (600 common shares issued to Excelsior Medical Co., Daewoong Pharmaceutical Co.)
- October 2011: Public stock offering of 1.4 billion yen (700,000 common shares issued)

#### Per Share Data

Per Share Data (Yen)	FY04/07	FY04/08	FY04/09	FY04/10	FY04/11	FY04/12
	Par.	Par.	Par.	Cons.	Cons.	Est.
No. of shares (Thousands)	4.7	7.0	7.0	8.5	9.5	
Earnings Per Share	-39,614.3	-39,414.9	-42,400.4	-7,870.6	-58,896.1	60.9
EPS (Fully Diluted)	-	-	-	-	-	
Dividend Per Share	0.0	0.0	0.0	0.0	0.0	0.0
Book Value Per Share	59,531.5	137,228.4	97,502.8	137,634.2	120,159.5	
Per Share Data (Yen, After Share Sp	it Adjustme	nts)				
Stock Split Adjustment Factor	400	400	400	400	400	
Split-Adjusted Shares (Thousands)	1,893	2,792	2,817	3,392	3,792	4,567
Earnings Per Share	-99.0	-98.5	-106.0	-19.7	-147.2	60.9
EPS (Fully Diluted)	-	-	-	-	-	
Dividend Per Share	0.0	0.0	0.0	0.0	0.0	0.0
Book Value Per Share	148.8	343.1	243.8	344.1	300.4	

Source: Company Data Processed by SR Inc.

Figures may differ from company materials due to differences in rounding methods.

The company has conducted the following stock splits:

- July 2011: Split shares 100:1 taking the outstanding common shares to 948,000.
- August 2011: Split shares 4:1 taking the outstanding common shares to 3,792,000.

### Warrants and Dilution

As of October 2011, there were outstanding warrants for 544,000 shares; some of these were subsequently exercised. However, as of end-January 2012, assuming all warrants were exercised that would take the number of outstanding common shares to 4,567,200, equivalent to 12% dilution.



### **Statement of Cash Flows**

Cash Flow Statement	FY04/07	FY04/08	FY04/09	FY04/10	FY04/11
(Million Yen)	Par.	Par.	Par.	Cons.	Cons.
Operating Cash Flow (1)	-	-	-	-28	-434
Investment Cash Flow (2)	-	-	-	-13	-18
Free Cash How (1+2)	-	-	-	-40	-452
Financial Cash Flow	-	-	-	573	498
Depreciation & Amortization (A)	-	-	-	75	79
Capital Expenditures (B)	-	-	-	-11	-10
Working Capital Changes (C)	-	-	-	-	1
Simple FCF (NI + A + B - C)	-	-	-	-	-467

Source: Company Data Processed by SR Inc.

Figures may differ from company materials due to differences in rounding methods.

### **Operating Cash Flow**

Almost fully determined by changes in pre-tax earnings.

### **Investment Cash Flow**

Minimal overall; driven by acquisition of tangible or intangible assets.

### **Financial Cash Flow**

Positive due to equity financing rounds.



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### **Other Information**

### **History**

The company was founded in May 2004 to develop, produce, and sell medical devices based on selfassembling peptide technology discovered by Dr. Shuguang Zhang of the Massachusetts Institute of Technology (MIT).

Dr. Zhang discovered self-assembling peptides at MIT in 1992. An MIT-research group acquired the rights to commercialize the technology from the university in May 2001, and established 3DM, Inc. (currently a subsidiary of the company) in the US. Nagano, who is the company chairman, teamed up with several people from Bain and Co. as angel investors to fund the startup. Confident in the technology behind self-assembling peptides, Nagano founded 3-D Matrix Japan Ltd. (now 3DM) in May 2004, with the aim, of developing, producing, and selling medical devices based on the platform in Japan and rest of Asia.

In October 2004 the newly formed subsidiary entered into a license-and-supply agreement with 3DM, Inc., and also obtained the rights to re-license the technology covered by the basic patents. 3DM, Inc. never took off the ground as a business, and in 2007 the Japanese subsidiary acquired its parent in a stock swap, resulting in the present corporate structure.

1992	Dr. Shuguang Zhang of MIT discovers self assembling peptides		
May 2001	3DM, Inc. (currently a subsidiary of the company) established in US as an MIT biotechnology venture		
April 2003	3DM, Inc. enters into an Exclusive Patent License Agreement (including sub-licensing		
	rights) for self organizing peptides with MIT, the patent owner		
May 2004	3-D Matrix Japan Ltd. founded to commercialize self-organizing peptide technology i Japan		
October 2004	<ul> <li>3-D Matrix Japan Ltd. concludes License and Supply Agreement* with 3DM, Inc. (currently US subsidiary), receiving licensing and sub-licensing rights for patents relating to self-assembling peptides</li> </ul>		
	<ul> <li>Agreements to supply research reagents free of charge to research institutions that had been entered into by 3DM, Inc. transferred to agreements between those research institutions and 3-D Matrix Ltd. (Japanese parent), and the company begins supplying them with PuraMatrix free of charge</li> </ul>		
October 2007	3DM, Inc. becomes a subsidiary of 3-D Matrix Japan Ltd.		
February 2008	worldwide rights to sell the PureMatrix product (RADA16) for research reagent		
March 2008	purposes Company name changed to 3-D Matrix Ltd. (3DM elsewhere in this report)		
October 2008	Patent application filed for using self-assembling peptides as a hemostatic agent in surgery		
April 2009	Itochu Chemical Frontier Corp. selected as partner for procurement of raw peptide materials and manufacture of products. Business Collaboration Agreement for advice, cooperation, and support signed		
July 2009	Exclusive Sales License Agreement signed with Fuso Pharmaceutical Industries Ltd. (Fuso Pharma) for the rights to sell its hemostatic agent for surgery product in Japan signed		
August 2009	Notification of clinical trial plan for hemostatic agent for surgery submitted to Japan's Pharmaceuticals and Medical Devices Agency (PMDA)		
January 2010	Clinical trials for hemostatic agent begin		
August 2010	Approval obtained for Class One medical devices manufacture and sale (Tokyo, Approval number 13B1X10105)		
September 2010	<ul> <li>3DM, Inc. submits IDE application for alveolar bone regenerator to FDA</li> <li>Partnership Agreement with Daewoong Pharmaceutical Co. of Korea granting them exclusive rights to sell hemostatic agent for surgery in Korea signed</li> </ul>		

<ul> <li>License Agreement with Taiwan's Excelsior Medical Co. granting them exclusive rights to develop, manufacture, and sell in Taiwan signed</li> </ul>		
<ul> <li>Agreement with Fuso Pharma for outsourced manufacturing of hemostatic agent for surgery signed</li> </ul>		
<ul> <li>Notification of conclusion of clinical trials for hemostatic agent for surgery submitted to PMDA</li> </ul>		
<ul> <li>Application for approval of manufacture and sale of hemostatic agent for surgery submitted to PMDA</li> </ul>		
3DM, Inc. receives IDE approval for alveolar bone regenerator from FDA		
Decision to establish European subsidiary in Lyon, France		
<ul> <li>Exclusive sales agreement with Fuso Pharma for mucous membrane protuberance material signed</li> </ul>		
<ul> <li>US clinical trials begin alveolar bone regenerator product, intended for dental implantation (registration and trial surgery for initial patients begins)</li> </ul>		

\* In April 2009, the company and 3DM, Inc. of America revised agreements as necessary to reflect the October 2007 conversion of 3DM, Inc. into a company subsidiary

### **News & Topics**

### **Top Management**

### Keiji Nagano, Chairman

Nagano was one of 3DM, Inc.'s (of America) original investors. In 2004 he sublicensed patents from it and established 3DM Japan. After working at Exxon and Bain & Co., he joined New Media in 2000, serving as the representative for New Media Japan Inc. At Bain and Co. he served as a vice president in their Tokyo office and had a central role in establishing Bain's Korea practice and served as the representative there for four years. While at Bain he worked with clients across a variety of industries, but accumulated particular experience in the telecoms, high-tech, entertainment, and healthcare fields. He has an MBA from Columbia University.

### Kentaro Takamura, President and CEO

Takamura worked for many years developing pharmaceuticals, biomaterials, and medical devices. He then went on to found Japan Tissue Engineering Co. (Jasdaq 7774) in 1999, which was the first company in Japan to develop products employing cultured human cells, and served as a director and head of R&D. He became COO of Medinet Co. (TSE 2370) in 2002, where he developed business support for cell tissue medical treatment and took the company public for its October 2003 listing on the Tokyo Stock Exchange's Mothers market. He has been a director of 3DM since 2005, and president since 2007. He has a PhD in medicine from Tokyo Medical University.

### Jun Okada, Director

Since 1998 Okada worked as a consultant in the Tokyo office of Bain & Co., where he was involved in many projects, including one year as a resident involved development support for a pharma company and venture capital investment support for biotech companies. In 2005 he took over management planning for 3DM and was appointed a director in 2007. He has a MBA from INSEAD.

### **Employees**

On a consolidated basis, the company had 20 employees as of end-August 2011. The parent had 18 of those (average age 39.8 years; years at the company 2.2 years).

The company has very little assets itself for the development, manufacturing, or sales of products, and these functions are outsourced to various external partners.



### **Major Shareholders**

Amount
Held
8.33%
6.29%
6.14%
4.29%
3.54%
3.54%
3.32%
2.78%
2.22%
2.22%

Source: Company Data Processed by SR Inc. (As of end-October 2010)

3DM Investment LLC is a fund backed by angel investors and MIT professors. It has been a shareholder of 3DM, Inc. of America since its founding. Other major shareholders of the company are business partners of the company, such as Fuso Pharmaceutical Industries Ltd. (TSE 4538).

### **Dividends and Shareholder Benefits**

Once the company's cumulative losses are cleared management will start considering whether or not to pay a dividend by looking at the company's financial situation and trends in performance.

### **Investor Relations**

The company plans to hold two results meetings annually following the release of its 1H and full year results.



### **By The Way**

### Glossary

### Absorption, Distribution, Metabolism, Excretion (ADME) Experiment

A pharmacokinetic experiment monitoring the entire process from the administration of a drug into the body through to its excretion from the body. ADME experiments gauge the resident period and excretion process and duration of a drug or equivalent in or from the body.

### Alanine (A)

A type of neutral protein-forming amino acid. A nonessential amino acid for humans, and commonly exists naturally in such foods as meats, soy beans, and dairy products. Abbreviated as A or Ala.

### Amino Acid

Compounds with an amine group (NH2) and a carboxylic acid group (-COOH) in the same molecule.

### Arginine (R)

A basic amino acid that forms proteins. It is a nonessential amino acid for humans, and commonly exists naturally in such foods as meats, soy beans, and dairy products. It is abbreviated to R or Arg.

### Artificial blood vessel replacement surgery

Surgery for improving blood flow by removing the blood vessel area where blood flow is hindered due problems such as an aneurysm, and replacing it with an artificial blood vessel composed of synthetic fibers.

### Asparaginic acid (D)

An acidic amino acid that forms proteins; it is a nonessential amino acid for humans, and commonly exists naturally in such foods as meats, soy beans, and dairy products. It is abbreviated to D or Asp.

### Basic fibroblast growth factor (bFGF)

Contributes to fibroblast growth and angiogenesis (the physiological process involving the growth of new blood vessels from pre-existing vessels) at the time of wounding.

### Bridging

The practice of sharing data for preclinical and clinical trials between countries with different drug regulations when applying for regulatory approval.

### Carrier

A substance that serves as the foundation for securing a substance that exhibits absorption or catalytic activity.

### **Clinical trial**

Tests for studying the safety and effectiveness of an unapproved drug or medical device on humans. The drug/device is administered to humans and data collected, for the purpose of obtaining regulatory approval for its commercial use.

### Coronary artery bypass graft surgery

A surgery treatment for ischemic heart disease (any disease characterized by reduced blood circulation to the heart), which restores blood blood-flow to the heart. Blood vessels are connected to the aorta in order to alleviate a lessening of blood-flow caused by contraction or blockage of the coronary artery sending blood from the heart.

### **Drug Delivery System (DDS)**

A device or technology that provides the necessary dosage of a drug over a required length of time.



### Embolization

Introducing substances into the circulatory system to cause blood vessel occlusion. Also, a minimally invasive therapeutic procedure using the technique.

### Endoscopic Mucosal Resection (EMR)

A surgical procedure for treating early stage cancers or polyps. A high frequency electrical current is targeted into the submucosal layer through a wire (known as a snare) using an endoscope, in order to avoid damage in the muscle or below (within the submucosal layer). The tumors/polyps are then recovered.

### Endoscopic submucosal dissection (ESD)

A relatively new surgical method for treating early stage stomach or throat cancer by using various electric scalpels to gradually carve away at the tumor after first injecting drugs such as hyaluronic acid in the area of the tumor and then creating a sufficient submucosal bulge. Since it uses an electric scalpel to cut away the tumor, it differs from endoscopic mucosal resection in that there is no limit on the size of the structure to be ablated, and it is possible to ablate an entire large lesion all at once.

### **Extracellular matrix**

A scaffold material that supports the adhesion and growth of cells and proteins that form collagen outside of cells.

### Exudative (oozing) bleeding

Hemorrhage in which blood flows weakly, in an oozing fashion.

### Fibrinogen

Fibrinous plasma protein; a blood clotting factor.

### Gelation

Gels are absorbent polymer materials that retain the flexibility of liquids while having the elasticity of solids. The formation of these materials is known as gelation.

### **Good Laboratory Practice (GLP)**

Code of practice for maintaining the reliability of data for preclinical trials (especially safety tests, such as animal experiments) for drug or medical device development.

### **Investigational Device Exemption (IDE)**

Application submitted to US Food and Drug Administration (FDA) for special exemption relating to clinical testing of new medical devices.

### Material Transfer Agreement (MTA)

An agreement relating to the use of research samples such as genes, lab animals, or antibodies, when they are being transferred to a third party researcher.

### **Milestone payment**

Payments made by a contract partner to a company that has invented a new product in accordance with the development progress for a new drug or medical device. The timing of these payments will be specified under any joint development agreement or exclusive sales licensing agreement between the companies.

### Occlusion coil / artificial embolization device

A medical device intended for blocking blood flow to a site when treating it, these are administered intravascularly, causing the formation of an embolism (blocking the blood vessel).



### Peptide

A chemical substance formed from two or more bonded amino acids (depending on the number of amino acids involved they may also be referred to as dipeptides, polypeptides, etc.).

### pН

A measure of alkalinity or acidity (concentration of hydrogen ions).

### **Platelet Derived Growth Factor (PDGF)**

Primarily contributes to regulation of growth, and migration of mesenchymal cells (fibroblasts, smooth muscle cells, glial cells, etc.).

### **Preclinical trial**

An experiment conducted during the research stage of the manufacturing authorization application process of a drug or medical device on multiple animals for obtaining scientific data for evaluating or proving the fundamental efficacy of a drug or medical device before using it on humans (clinical trial).

### **Pre-filled syringe**

A syringe sold ready-to-use, filled with the required drug dosage.

### PuraMatrix™

A first generation hydrogel product employing self-organizing peptide technology. Repeated sequences of peptide RADA16, formed from the amino acids arginine (R), alanine (A), asparaginic acid (D), which comprise the body.

#### **Reimbursement Price**

The price set by the Ministry of Health, Labour and Welfare for medical devices covered by national health insurance.

### Scaffolding

An intracellular matrix composed of a substance found within the body, such as collagen, which acts as a scaffold for cell growth.

### Self-assembling peptide

A peptide family that collects with other peptide molecules, and forms nanofibers under certain physiological conditions (neutral pH and the presence of salts).

#### siRNA

Low molecular weight double-stranded RNA composed of 21-23 base pairs. siRNA contributes to the phenomena known as RNA interference (RNAi) and suppresses gene expression in a sequence-specific fashion by breaking down messenger RNA (mRNA).

### Surfactants

A substance that lowers the surface tension of a liquid in small quantities.

### **Upfront Payment**

A payment made by a licensee to the licensor at the beginning of a license contract.



### April 25, 2012

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