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Building on principles

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Mirae Asset Daewoo Co., Ltd.

[Pharmaceuticals/Biotech]

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TissueGene
(Unlisted/Not Rated)

Aiming for DMOAD designation

- TissueGene is a biotech company currently developing an osteoarthritis therapy called Invossa
- Invossa is positioned to bridge treatment gap
- Receiving DMOAD designation by proving structural improvement will be key
- Additional licensing deals could drive up Invossa's value over the medium-to-long term

Biotech company focused on developing osteoarthritis therapy

TissueGene, which is set to go public on the KOSDAQ on November 6th, is a biotech company currently developing a gene and cell therapy for osteoarthritis called Invossa. Invossa consists of a mixture of unmodified and modified human chondrocytes engineered to produce the growth factor TGF-ß1, which is injected into the knee joint to treat osteoarthritis. Following approval from the Korean Ministry of Food and Drug Safety (MFDS) on July 12th, the therapy is ready to go on sale in the domestic market. In the US, the company has received FDA acceptance for its Investigational New Drug (IND) application (Phase 3 clinical study), and aims to begin patient injection in 1H18, submit a Biologics License Application (BLA) in 2021, obtain approval in 2022, and achieve commercialization in 2023.

The price range of the company's IPO has been set at W16,000-27,000 per depository receipt (DR), which would put the company's market value at W1.01-1.71tr. Based on the low end (W16,000) of the price range, the company is expected to raise W120bn, most of which will be used to fund the US Phase 3 trial for Invossa.

Invossa positioned to bridge treatment gap

We believe Invossa is competitively positioned, as the therapy targets a treatment gap that exists between conventional drugs (pain medication and hyaluronic acid injections) and joint replacement surgery. Patients with osteoarthritis are typically treated with physical therapy or lifestyle modifications during the early stages of the disease, pain medication or hyaluronic acid injections during the middle stages, and joint replacement during the late stages.

However, middle-stage treatment options only offer temporary pain relief and fall short of providing fundamental treatment. Pain medications can also cause gastrointestinal side effects, while recent studies have shown hyaluronic acid injections to be ineffective. Meanwhile, late-stage treatments (joint replacement surgery) can be burdensome for patients, due to their high costs and rehabilitation requirements.

We think Invossa could offer a more effective treatment for middle-stage patients, while allowing late-stage patients to hold off surgery for some time. It appears as though the therapy has the potential to create new demand.

FY (Dec.)	2015	2016	1H17
Revenue (Wbn)	0	13	-
OP (Wbn)	-3	6	-6
OP margin (%)	-1059.4	45.1	-
NP (Wbn)	-6	7	-4
EPS (W)	-1,822	2,112	-754
ROE (%)	-349.5	33.8	-22.4
P/E (x)	-	-	-
P/B (x)	-	-	-
Dividend yield (%)	-	-	-

Note: All figures are based on non-consolidated K-IFRS
Source: Company data

Receiving DMOAD designation by proving structural improvement will be key

A disease-modifying osteoarthritis drug (DMOAD) refers to a fundamental osteoarthritis treatment that has the potential to reduce symptoms by improving joint structures or delaying the progression of the disease. Invossa's Korean Phase 3 trial proved the therapy's efficacy in improving function and reducing pain, but failed to demonstrate statistically significant structural improvement (although a tendency was observed).

In the forthcoming US Phase 3 trial, the company is seeking to gain DMOAD designation by improving the trial's protocols. Unlike the Korean study, the US trial will follow patients for two years (versus one year for the Korean study), expand the patient criteria to Kellgren and Lawrence Grade (KLG) 2 and 3 (versus KLG 3), and enroll 1,020 patients (versus 159) to prove statistical significance. Notably, the Korean study has already demonstrated the possibility of structural improvement in key measures of the MRI assessment, including bone marrow edema, and the volume/thickness of cartilage damage.

Additional licensing deals may drive up Invossa's value over mid-to-long term

Last year's Japanese licensing deal offers clues about Invossa's potential value in developed markets. In November 2016, Mitsubishi Tanabe Pharma signed a W498.9bn deal for the Japanese rights to Invossa, which included a W27.3bn up-front payment (the total figure does not include running royalties). According to market researcher GlobalData, Japan's knee osteoarthritis market is estimated at US$257mn in 2017, while the US and five major European countries are estimated to have a combined market of US$1.33bn. Based on these figures, an Invossa licensing deal covering the US and five major European countries could be worth roughly W2.58tr in milestones. If such a deal were signed, it would be the second-largest in Korean history—behind only Hanmi Pharmaceutical's 2015 deal with Sanofi (valued at W5tr)—and the largest by far for a single asset (with the Hanmi-Sanofi deal involving three pipeline assets).

That said, it should be noted that Invossa's release in developed markets is still years away (2023), and that it will be difficult to predict the actual timing of the deal. Through 2022, TissueGene is expected to mainly derive its earnings from: 1) a 2% royalty on Kolon Life Science's Invossa sales and 50% milestone on sub-licensing deals; and 2) the drugstore and cosmetic businesses, which were recently acquired from a group affiliate. The company expects to record revenue of W19.5bn and an operating loss of W6.3bn in 2022, according to its prospectus.

Table 1. Osteoarthritis therapy treatments by stage

Stage	Treatment	Limitations
Early	Improve life habits, physical therapy	Unable to modify disease
Mid	Analgesics, HA injections	Unable to modify disease, temporary pain ease, drug side effects
	Treatment gap	
Late	Artificial joint replacement surgery	High cost, anesthesia, rehabilitation required

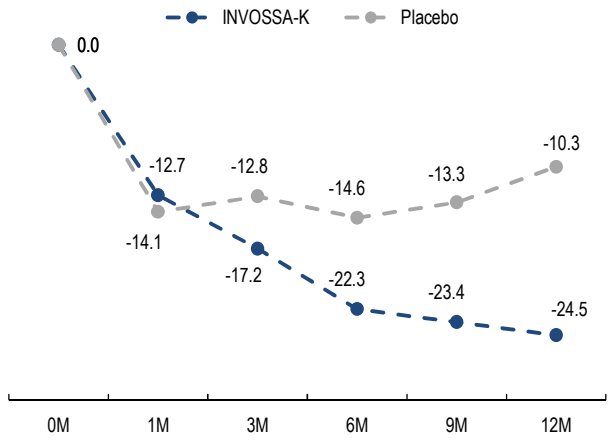
Source: Mirae Asset Daewoo Research

Table 2. Phase 3 clinical trial protocols in US and Korea

		US	S. Korea
Trial design		Randomization, double-blind, placebo, multicenter	
Site		70 in US	12 in S. Korea
Enrollment		1,020	159
Patient pool		INVOSSATM: 680 / Placebo: 340	INVOSSA-K: 78 / Placebo: 81
K&L Grade		Grade 2 or 3	Grade 3
Period		24M	12M
Endpoints	Primary endpoint	VAS, WOMAC1	IKDC, VAS
	Secondary endpoint	X-Ray [JSW2], IKDC [MRI, Liquid Biomarker] 4	WOMAC, KOOS3, MRI, X-Ray [JSW], Biomarkers
Claim range		Primary endpoint, Secondary endpoint	Primary endpoint

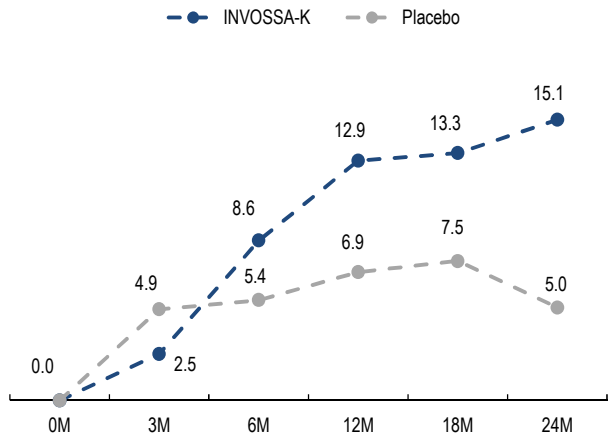
Note:
1) WOMAC (Western Ontario and McMaster Universities Osteoarthritis Index): Widely used set of standardized questionnaires used by health professionals to evaluate the condition of patients with osteoarthritis of the knee and hip, including pain, stiffness, and physical functioning of the joints.
2) JSW (Joint Space Width): Measurement of cartilage thickness in osteoarthritis of the knee
3) KOOS (Knee Injury and Osteoarthritis Outcome Score): An instrument to assess a patient's opinion about their knee and associated problems
Source: Mirae Asset Daewoo Research

Figure 1. Invossa-K's VAS score change in Korean Phase 3 trials



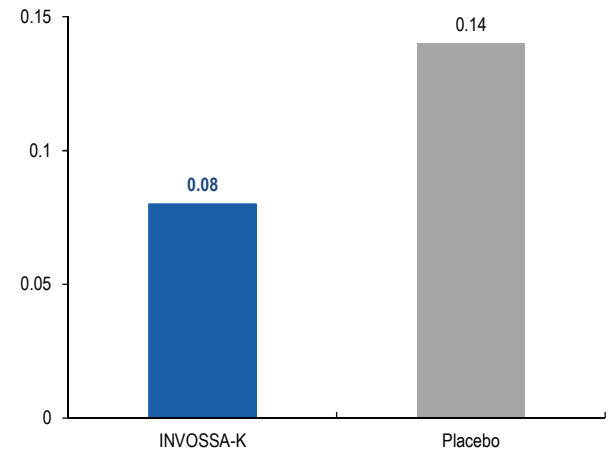
Source: TissueGene, Mirae Asset Daewoo Research

Figure 2. Invossa-K's IKDC score change in Korean Phase 3 trials



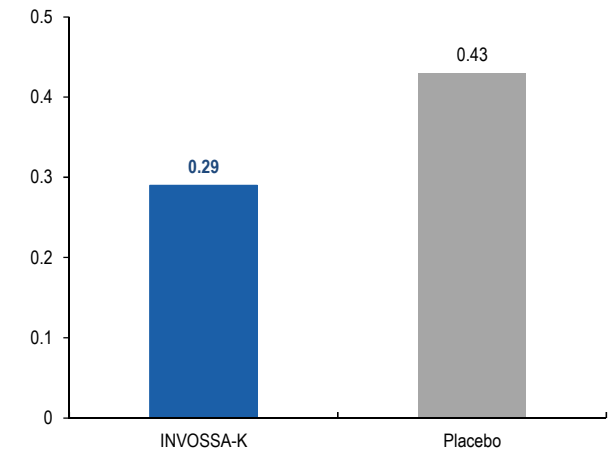
Source: TissueGene, Mirae Asset Daewoo Research

Figure 3. Cartilage damage volume in Korean Phase 3 trials



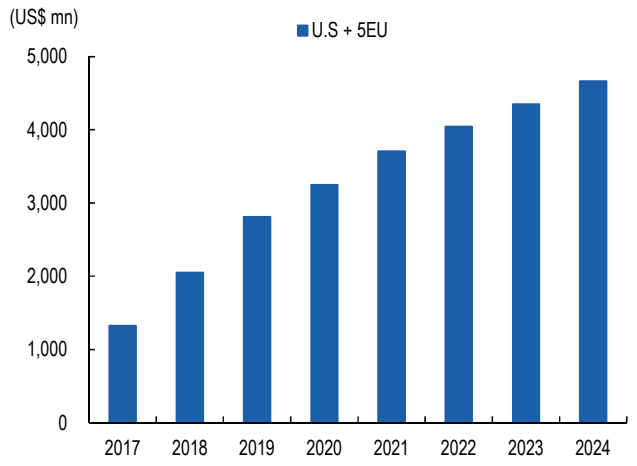
Source: TissueGene, Mirae Asset Daewoo Research

Figure 4. Cartilage damage thickness in Korean Phase 3 trials



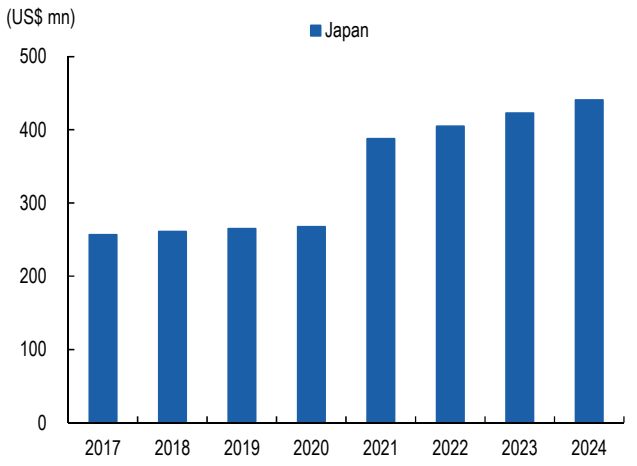
Source: TissueGene, Mirae Asset Daewoo Research

Figure 5. Knee osteoarthritis market trend of US and 5 EU countries



Note: 5EU (France, Germany, Italy, Spain, UK)
Source: TissueGene, Mirae Asset Daewoo Research

Figure 6. Japanese knee osteoarthritis market trend



Source: TissueGene, Mirae Asset Daewoo Research

Table 3. Estimated financial statement

(Wmn)

	2017F	2018F	2019F	2020F	2021F	2022F	2023F
Revenue	8,397	10,207	10,270	11,172	17,627	19,515	704,637
OP	-8,168	-8,035	-9,802	-8,163	-2,321	-6,261	239,790
NP before tax	-9,276	-9,298	-10,779	-8,813	-2,647	-6,302	239,790
NP	-9,276	-9,298	-10,779	-8,813	-2,647	-6,302	187,115

Source: TissueGene, Mirae Asset Daewoo Research

APPENDIX 1

Equity Ratings Distribution & Investment Banking Services

	Buy	Trading Buy	Hold	Sell
Equity Ratings Distribution	74.52%	12.50%	12.98%	0.00%

* Based on recommendations in the last 12-months (as of September 30, 2017)

	Buy	Trading Buy	Hold	Sell
Investment Banking Services	70.73%	17.07%	12.20%	0.00%

* Based on recommendations in the last 12-months (as of June 30, 2017)

Disclosures

Mirae Asset Daewoo Co., Ltd.`s analyst attended the IR meeting held by TissueGene within recent one month. Expenses related to the meeting were covered by TissueGene.

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