Trinity Delta

Futura Medical

Update

Remarkable data from pivotal trial opens new possibilities

11 December 2019

Futura Medical has presented details of the pivotal Phase III study (FM57) results for its lead compound, MED2005. All doses achieved all primary endpoints against baseline (p<0.001) throughout the 12-week period, with secondary endpoints also being met. However, the placebo arm, consisting of the DermaSys formulation alone, achieved similarly impressive results. Dose-dependent variation in side-effects should allay fears that administration errors may be to blame. These data suggest that the DermaSys gel alone has a significant clinical effect across the three severities of ED (Erectile Dysfunction) examined. Clearly the data needs to be digested, but this would appear to open up new opportunities, especially in terms of regulatory pathways, patent life, and commercial potential. Until we have greater visibility, we suspend our valuation and forecasts; for context we valued Futura Medical at £127m (62p a share).

Year-end: December 31	2017	2018	2019E	2020E
Sales (£m)	0.4	0.0	0.0	-
Adj. PBT (£m)	(4.8)	(7.2)	(10.4)	-
Net Income (£m)	(3.9)	(5.9)	(8.6)	-
EPS (p)	(3.2)	(4.5)	(4.2)	-
Cash (£m)	8.4	9.2	1.5	-
EBITDA (£m)	(4.8)	(7.2)	(10.4)	-

Source: Trinity Delta Note: Adjusted PBT excludes exceptionals, Cash includes short-term investments.

- **Unequivocal results create confusion** Headline data from the 1,000-pt pivotal Phase III FM57 trial is highly significant (p<0.001) and clinically meaningful vs baseline across all three glyceryl trinitrate (GTN) treatment arms and the DermaSys placebo arm for all three primary endpoints (IIEF-EF, SEP2 and SEP3). No difference between study arms was detected from an efficacy standpoint; however, dose-dependent side-effects were seen, suggesting no formulation/administration errors.
- **Potential to pursue medical device regulatory pathway** The FM57 data suggests that the DermaSys formulation alone has a comparable effect to all GTN doses studied, opening an approval pathway in ED via the simpler, potentially faster medical device route in the US and Europe. Initial company assessments indicate that the bar for clinical evidence may already be met; although this is yet to be confirmed by the respective regulators. Some small studies may be required.
- **Clinical data highlights commercial attractive product profile** DermaSys alone compares favourably with current ED therapies, with rapid speed of onset (within 10 minutes), efficacy approaching that of PDE5s (Cialis) but with cleaner safety, no contraindications (no GTN), and potential for PDE5 combination use. It could be unique as a topical applied to the glans penis that is clinically proven to treat ED.
- **Valuation and forecasts suspended** The remarkable FM57 results have created understandable uncertainty and, until we have greater visibility, we are obliged to suspend our valuation and forecasts (post FY19). There are clear opportunities, not least in terms of patent life and market opportunities, but equally there are potential unknowns that may unexpectedly crop up to dampen our enthusiasm. For context, our last published valuation was £127m (equivalent to 62p/share).

Price	14.75p
Market Cap	£30.2m
Enterprise Value	£24.6m
Shares in issue	205m
12 month range	5.65-49.2p
Free float	70.4%
Primary exchange	AIM
Other exchanges	N/A
Sector	Healthcare
Company Code	FUM
Corporate client	Yes

Company description

Futura Medical is an R&D driven small pharma company, with a novel DermaSys transdermal delivery platform. The lead programme, MED2005, is a topically applied gel that is in Phase III trials for erectile dysfunction (ED). A pain relief gel, TPR100, is awaiting UK approval.

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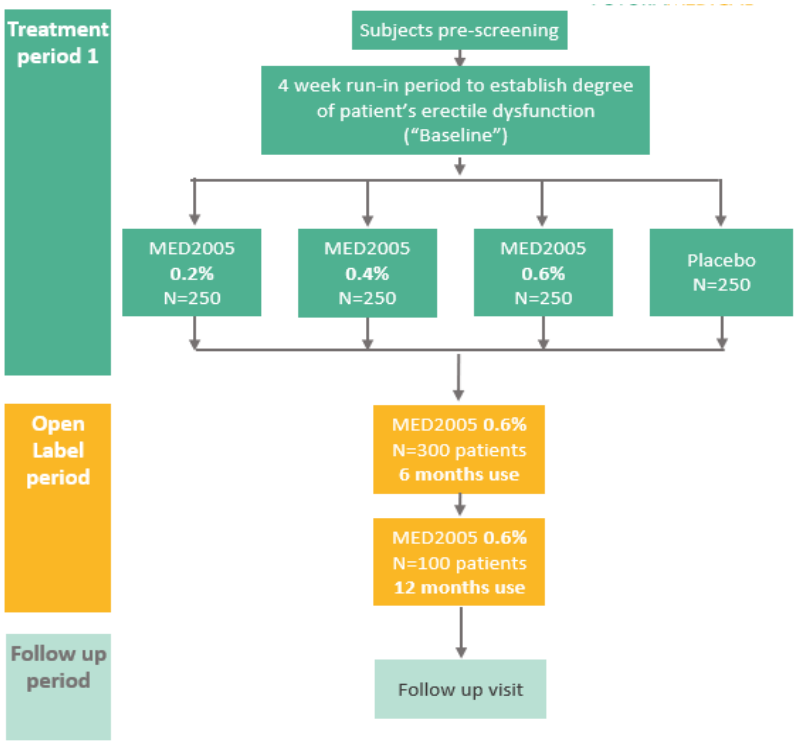
Futura Medical: uncertainties and opportunities

Futura Medical has provided more detail on the data from the pivotal Phase III study (FM57) for its lead compound MED2005. The headline results show impressive and consistent improvements across all the primary endpoints for all doses at 12 weeks vs baseline. These are highly statistically significant (p<0.001) and clinically meaningful. Secondary endpoints are similarly positive. These otherwise excellent data are confusing because the same results are seen with the DermaSys placebo arm. The side-effect profile of the treatment arms suggests no formulation or administration error has occurred; which in turn means that FM57 has shown that DermaSys used alone is a potent and effective treatment for all severities of Erectile Dysfunction (ED). This opens new avenues to be explored, including a potentially simpler and faster regulatory route to market, fresh patent protection, as well as new commercial options.

DermaSys formulation alone is a potent and effective treatment

The headline data from the pivotal Phase III FM57 study of MED2005 in ED showed a remarkably strong and consistent effect in all four arms, three active and one placebo, with highly statistically significant (p<0.001) improvements from baseline across Mild, Moderate, and Severe forms of ED. However, there is a lack of differentiation between any of the active arms and placebo; which would indicate that the action of the proprietary DermaSys formulation alone has an effect comparable to the glyceryl trinitrate (GTN) doses studied. Importantly, the dose-dependent variation in side-effects, notably the headaches typically associated with GTN dosing, should allay fears that administration, formulation, or procedural errors may be to blame for these outcomes.

Exhibit 1: FM57 study design



Source: Futura Medical

Positive results across all four study arms, including placebo

The FM57 study consisted of three active arms, with gel doses of 0.2%, 0.4%, and 0.6%, and a placebo arm (DermaSys formulation alone) run in parallel. The study involved 1,000 males aged 18-70, with 250 in each arm, who had confirmed clinical diagnosis of erectile dysfunction (defined as an IIEF score of less than 25) for at least three months. They undertook a four-week run-in period, which established a baseline, followed by 12 weeks of treatment.

Primary endpoints are broad and clinically relevant

The primary efficacy endpoint was based on the erectile function domains of the IIEF questionnaire, but with SEP2 and SEP3 questions from the Sexual Encounter Profile (SEP) questionnaire (assessing achievement of erection and the ability to complete sexual intercourse). Secondary endpoints include responder analysis, subjective measures of the time of onset and duration of action (erection), additional questions on usage and application, and safety/adverse event profile.

Exhibit 2: FM57 headline results – primary endpoints (change from baseline)

Primary Endpoints	DermaSys®	P-values	0.6mg (0.2%) MED2005	P-values	1.2mg (0.4%) MED2005	P-values	1.8mg (0.6%) MED2005	P-values
IIEF-EF Domain	3.60	<0.001	3.39	<0.001	3.42	<0.001	3.66	<0.001
SEP2 (Were you able to insert your penis into your partner's vagina)	13.8%	<0.001	9%	<0.001	13.27%	<0.001	10.67%	<0.001
SEP3 (Did your erection last long enough for you to have successful intercourse)	23.16%	<0.001	20.76%	<0.001	22.63%	<0.001	23.27%	<0.001

Source: Futura Medical

The results for the primary endpoints are shown in Exhibit 2 above. These highlight the highly significant ($p<0.001$) and consistent improvements against baseline, but with no statistical difference between the active arms and the placebo control. These results are for the 12-week analysis but the data from the four and eight week assessments were broadly similar. The outcomes for the secondary endpoints such as efficacy, speed of onset, and duration of action showed the same pattern and were also similarly consistent.

Interestingly, a 'placebo-effect' was seen in the four-week FM53 study, although the hypothesis at the time was that the study not long enough to see clear separation between the active (0.2% GTN) and placebo (DermaSys) arms.

Improvement seen in all ED patient groups, including severe

Exhibit 3 shows the results for the clinically important difference using the Rosen & Araujo criteria. Again, we see consistent results with a statistically significant improvement in erectile function across 'pooled' patient severities (mild, moderate, and severe) of erectile dysfunction against baseline across the three treatment arms and placebo. Over 60% of all patients experienced a meaningful difference in improvement of their erections using recognised assessment techniques. Interestingly, shown in the green box, the responses across all three primary endpoints were similar across the mild, moderate, and severe ED groups in the placebo arm (treated with DermaSys alone).

Exhibit 3: FM57 headline results – clinically important differences

- Clinically Important Differences at 12 weeks (Rosen & Araujo) – Percentage of patients who noticed a meaningful difference
- Highly positive results from a clinically meaningful perspective

(%)	DermaSys®	0.6mg (0.2%) MED2005	1.2mg (0.4%) MED2005	1.8mg (0.6%) MED2005
IIEF	63	64	62	70
SEP2	75	72	74	73
SEP3	68	67	67	70

(%)	DermaSys® - Responders in patients with Mild/Moderate/Severe ED using Rosen/Araujo
IIEF	61 / 59 / 80
SEP2	83 / 57 / 77
SEP3	71 / 61 / 71

Source: Futura Medical

Exhibit 4 details the side-effect profile seen with the three MED2005 doses and the DermaSys placebo arm. Although the aim of the slide was to show MED2005's attractive profile and to compare, indirectly, its safety profile with Cialis (tadalafil), for us the real importance of this data lies in the data for headaches seen in FM57.

Exhibit 4: FM57 headline results – adverse events summary

Adverse events	DermaSys® (N=250)	0.6mg (0.2%) MED2005	1.2mg (0.4%) MED2005	1.8mg (0.6%) MED2005	Adverse events - Cialis® [1]	Cialis® 5mg (N= 151) [1]
Headache	3%	11%	10%	17%	Headache	11%
Flushing	-	0.4% [2]	-	-	Flushing	2%
Nasal congestion	-	0.8% [2]	0.4% [2]	0.4% [2]	Nasal Congestion	2%
Back pain	-	-	-	0.4% [2]	Back pain	3%
Dizziness	-	-	-	0.8% [2]	Myalgia	2%
Penile Burning	1%	1%	2%	6%	Pain in limb	1%

Source: Futura Medical Note: 1 – for illustrative purposes only as data is derived from different clinical studies, Cialis US Prescribing information , 2018; 2 – numbers below 1% have not been rounded

Side-effect data suggests the integrity of FM57 is sound

Whenever a well-structured and planned clinical trial throws up such remarkable results the first question should be whether something has gone awry in the study execution. Examples would include formulation errors, administration issues, and problems with data collection and processing. However, the clear dose response seen in the headache side-effect, a well-recognised problem with GTN administration, suggests that the study was performed correctly, and that the data are valid. This would mean that the DermaSys formulation alone is a potent and effective treatment for all forms of ED.

New horizons opening or back to the drawing board?

There are several positives arising from the FM57 data

Clearly, these results have created an understandable amount of confusion and uncertainty. Yet if the DermaSys formulation was indeed shown to be the causative factor underlying such clinical improvements then several potentially positive outcomes would arise such as:

- Being classed as a medical device rather than a pharmacological treatment means a simpler, and faster regulatory pathway as no further clinical work would be required for the EU and only a small local study in the US;
- A larger commercial opportunity as there would be no contraindications for patients taking cardiovascular medications (eg nitrates and alpha-blockers) and it could be used in combination with other ED therapies such as the PDE5s;
- The efficacy seen in FM57 suggests an activity level higher than niche products such as Vitaros (a topical gel which is applied into the urethra) and approaching that of the oral PDE5s such as tadalafil, but with a faster onset of action (60% of patients seeing erection onset within 10 minutes of application) and fewer side-effects;
- Although we expect the first launches would be as prescription-only (Rx) treatments there is an opportunity to achieve a faster and easier switch to OTC status in many geographic markets, if commercially prudent;
- Opportunistically, management has already filed new patent applications to cover the ED indication and that could potentially extend the IP protection through to 2039.

Partnering discussions and longer-term plans likely delayed

On the downside, the new data will take time to digest and, assuming it is found to stand, it will delay any longer-term planning until there is greater clarity and visibility. This will apply particularly to out-licensing and partnering discussions.

Valuation and Financials

The remarkable results from the FM57 study have created understandable uncertainty and until we have greater visibility, we are obliged to suspend our valuation and forecasts post the financial year ending December 2019.

Valuation and post-FY19 forecasts suspended as assumption need to be revisited

Our previous DCF model, which assessed the rNPV of each clinical programme, with MED2005 split into prescription-only (Rx) and over-the-counter (OTC) scenarios for both Europe and the US, was based on numerous assumptions which will need to be revisited for DermaSys for ED, including, but not limited to: potential launch timing; market size; growth rates; R&D spend; patent life; Rx to OTC switching; and commercial strategies of likely future partners.

There are clear opportunities, not least in terms of patent life and market opportunities, but equally there are potential unknowns that may unexpectedly crop up to dampen our enthusiasm. For context, our last published current valuation was £127m (equivalent to 62p/share).

Similarly, we suspend our FY20 and FY21 financial forecasts. For FY19 we expect R&D spend of £9.35m (associated with the FM57 study and preparatory work for FM59) with G&A for the full year of £1.08m. On this basis we forecast an EBITDA of £10.4m and net loss of 8.6m (4.2p per share).

Potential medical device regulatory pathway has repercussions for timelines and funding need…

Beyond FY19, anticipated R&D expenditure will fall as the FM59 study will no longer be pursued, although there will be costs associated with the close out of the open label phase of FM57, and potentially in connection with other smaller studies that may be required by regulators (most likely the FDA). Of clear interest to investors is the fact that a second pivotal Phase III trial (FM59) is no longer required, and this has repercussions for the quantum of Futura Medical's funding needs. In our previous note, we had highlighted that FM59 required funding to be in place ahead of the start of recruitment in 2020. We had assumed the study would cost c £7m, with the company targeting a c £10-15m injection of funds (potentially through out-licensing/partnerships, equity, debt, or a hybrid). Our assumptions around Futura Medical's funding requirement rests on the regulatory pathway for DermaSys for ED, and we await further guidance.

….we await further updates from the company

The largest single element of spend remains the costs of filings for the approvals of DermaSys for ED in the various regulatory regions. At present, the regulatory timeline and timeframe is unknown; management are seeking meetings with the US and European regulators and will provide an update on what they "believe will be a simple and expected lower cost regulatory pathway as soon as possible".

Exhibit 5: Summary of historic financials and our previous estimates

Year-end: December 31 £'000s	2017	2018	2019E	2020E	2021E
INCOME STATEMENT					
Revenues	**363**	**0**	**0**	**0**	**0**
Cost of goods sold	0	0	0	0	0
Gross Profit	**363**	**0**	**0**	**0**	**0**
R&D expenses	(4,100)	(6,039)	(9,346)	(8,556)	(4,962)
General and administrative expenses	(1,118)	(1,228)	(1,084)	(1,583)	(1,706)
Underlying operating profit	**(4,856)**	**(7,266)**	**(10,430)**	**(10,139)**	**(6,669)**
Other revenue/expenses	0	0	0	0	0
EBITDA	**(4,843)**	**(7,247)**	**(10,411)**	**(10,115)**	**(6,643)**
Operating Profit	**(4,856)**	**(7,266)**	**(10,430)**	**(10,139)**	**(6,669)**
Interest expense	19	28	19	(1)	17
Profit Before Taxes	**(4,837)**	**(7,239)**	**(10,411)**	**(10,140)**	**(6,652)**
Adj. PBT	**(4,837)**	**(7,239)**	**(10,411)**	**(10,140)**	**(6,652)**
Current tax income	936	1,358	1,836	1,925	1,117
Cumulative preferred stock dividend	0	0	0	0	0
Net Income	**(3,900)**	**(5,881)**	**(8,574)**	**(8,215)**	**(5,535)**
EPS (p)	**(3.2)**	**(4.5)**	**(4.2)**	**(4.0)**	**(2.7)**
Adj. EPS (p)	**(3.2)**	**(4.5)**	**(4.2)**	**(4.0)**	**(2.7)**
DPS (p)	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
Average no. of shares (m)	120.6	131.9	204.7	204.7	204.7
Gross margin	*100%*	*N/A*	*N/A*	*N/A*	*N/A*
BALANCE SHEET					
Current assets	**9,541**	**10,830**	**3,856**	**10,711**	**5,247**
Cash and cash equivalents	8,363	9,158	1,473	8,390	3,129
Accounts receivable	181	306	98	98	98
Inventories	70	8	8	8	8
Other current assets	927	1,358	2,276	2,214	2,012
Non-current assets	**64**	**47**	**64**	**86**	**111**
Property, plant & equipment	64	47	64	86	111
Other non-current assets	0	0	0	0	0
Current liabilities	**(499)**	**(2,026)**	**(3,535)**	**(18,535)**	**(18,535)**
Short-term debt	0	0	0	(15,000)	(15,000)
Accounts payable	(499)	(2,026)	(3,535)	(3,535)	(3,535)
Other current liabilities	0	0	0	0	0
Non-current liabilities	**0**	**0**	**0**	**0**	**0**
Long-term debt	0	0	0	0	0
Other non-current liabilities	0	0	0	0	0
Equity	**9,106**	**8,852**	**385**	**(7,739)**	**(13,178)**
Share capital	44,913	50,393	50,412	50,412	50,412
Other	(35,807)	(41,541)	(50,028)	(58,151)	(63,590)
CASH FLOW STATEMENTS					
Operating cash flow	**(4,155)**	**(4,680)**	**(7,669)**	**(8,037)**	**(5,211)**
Profit before tax	(4,837)	(7,239)	(10,411)	(10,140)	(6,652)
Non-cash adjustments	195	140	87	117	105
Change in working capital	(385)	1,464	1,718	0	0
Interest paid	19	28	19	(1)	17
Taxes paid	851	927	918	1,987	1,319
Investing cash flow	**(56)**	**(5)**	**(35)**	**(46)**	**(51)**
CAPEX on tangible assets	(56)	(5)	(35)	(46)	(51)
Other investing cash flows	0	0	0	0	0
Financing cash flow	**221**	**5,480**	**19**	**15,000**	**0**
Proceeds from equity	221	5,480	19	0	0
Increase in loans	0	0	0	15,000	0
Other financing cash flow	0	0	0	0	0
Net increase in cash	**(3,990)**	**795**	**(7,685)**	**6,917**	**(5,262)**
Cash at start of year	12,353	8,363	9,158	1,473	8,390
Cash at end of year	**8,363**	**9,158**	**1,473**	**8,390**	**3,129**
Net cash at end of year	**8,363**	**9,158**	**1,473**	**(6,610)**	**(11,871)**

Source: Company, Trinity Delta Note: Adjusted numbers exclude exceptionals. The funding requirement is shown as short-term debt in FY20e, until transaction type, source and size are confirmed.

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