Trinity Delta

Futura Medical

Outlook

Nearing the critical point in Erectile Dysfunction

2 June 2020

Futura Medical is approaching a key point as the first of the regulatory filings for its novel erectile dysfunction (ED) treatment, MED3000, is expected within the next few months. MED3000 is a fast-acting gel that has proven clinical efficacy, a fast onset of action, and an attractive commercial profile. The ED market opportunity is sizeable, especially once MED3000 becomes widely available over the counter (OTC). Optimally addressing the various elements of the demographic segments and needs of the different geographies will, in our view, require careful selection of commercial partners. We expect the partnering discussions to start in earnest once the status of the regulatory approvals is known. Our DCF-based model, using conservative assumptions, values Futura Medical at £153.8m, equivalent to 60.9p a share.

Year-end: December 31	2018	2019	2020E	2021E
Sales (£m)	0.0	0.0	0.0	0.0
Adj. PBT (£m)	(7.2)	(11.1)	(4.8)	(3.9)
Net Income (£m)	(5.9)	(8.9)	(4.0)	(3.9)
EPS (p)	(4.5)	(4.4)	(1.6)	(1.3)
Cash (£m)	9.1	2.5	1.0	3.1*
EBITDA (£m)	(7.2)	(11.1)	(4.8)	(3.9)

Source: Trinity Delta Note: Adjusted PBT excludes exceptionals, Cash includes short-term investments. *FY21e cash includes assumed additional funding of £5m

- **MED3000 is safe and effective in ED** Detailed analysis of the pivotal FM57 data shows remarkably consistent outcomes for MED3000 across all treatment groups. There are clear and statistically meaningful improvements for the three co-primary endpoints, and also statistical superiority over baseline for Mild, Moderate, and Severe forms of ED (erectile dysfunction). The results are consistent when viewed across patient groups, study centres, geographies, and CROs performing the trial.
- **Regulatory filings expected in H220** Encouraging discussions with regulators in Europe and the US indicate that management targets of first submission in Europe by end-July, followed by a Q320 filing in the US, are realistic. Although difficult to gauge, MED3000's clinical profile, particularly the clean safety data, suggests a rapid transition to OTC status is probable. With activity approaching that of oral PDE5s such as tadalafil (Cialis), but with a faster onset of action and fewer side-effects, the commercial potential of MED3000 could be sizeable.
- **Partnering needs careful consideration** The complexities of the ED demographic segments, coupled with differing geographic marketing requirements, means that partnering discussions will not be straightforward. We believe no suitable global company exists, and a collection of strong regional players will likely provide the optimal commercial coverage. We would not expect meaningful dialogues with likely partners to advance until the regulatory status in each market is clearer.
- **Under-valued and relatively low-risk** We value Futura Medical using a risk-adjusted DCF model. We expect to revisit our assumptions as regulatory progress is achieved and visibility of the commercialisation strategies improves. Our current valuation is £153.8m (60.9p/share).

Price	21.75p
Market Cap	£53.4m
Enterprise Value	£41.8m
Shares in issue	245.6m
12 month range	7.16-47.9p
Free float	62%
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, a topically applied gel (MED3000), is approaching regulatory approval as a medical device for ED (erectile dysfunction) in Europe and the US.

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Investment case

Firmly focussed on erectile dysfunction opportunities

Futura Medical has developed a proprietary transdermal delivery platform known as DermaSys. This drives an active drug rapidly through the skin, achieving high concentrations with minimal residual effects. A number of potential applications have been explored, but a strategic review in 2018 decided to focus resources on two programmes: MED2005, a topical GTN gel for treating erectile dysfunction (ED); and TPR100, a topical diclofenac pain relief gel.

A pivotal Phase III trial (FM57) produced remarkable results that demonstrated the DermaSys formulation employed as a placebo had equivalent efficacy to MED2005. This formulation, now known as MED3000, is being developed as an ED treatment and will be submitted for US and European approval as a medical device during H220. Futura Medical will seek partners for MED3000 commercialisation. Futura Medical was founded in 1997, listed on AIM in 2003, and is based in Guildford, Surrey. It has 15 full time employees.

Valuation

Several value inflection points expected over the next year

As an early-stage development company, Futura Medical is well-suited to a DCF-based valuation. We calculate a risk-adjusted net present value (rNPV) of the lead projects - principally MED3000 - adjust them for success probabilities (clinical, regulatory, and commercial), sum them, and net this against costs. We always seek to adopt conservative assumptions, and this can be seen in the adoption curves and penetrations used within the market potential for MED3000. Despite this, our model results in a current valuation of £153.8m, or 60.9p per share (fully diluted). We would expect to revisit our assumptions as the MED3000 approval pathways progress, and the visibility of the commercialisation strategy improves.

Financials

Tight cost control and funding in place for registrations

Futura Medical had net cash of £2.51m at end-December 2019, raised £3.25m (gross) in January, and has a £2.2m R&D tax credit due in August. The lean nature of the company structure means that central costs are low, c £2.5m pa, with the majority of the spend now being the MED3000 registration processes in Europe and the US. Assuming no surprises, the cash runway currently extends to Q221.

Sensitivities

Main risks centre on MED3000 approval and commercialisation but are reasonably contained

Being a small loss-making healthcare company the typical industry risks apply. However, reflecting its current stage of development, Futura Medical's risk profile is now lower. The key sensitivities relate to successfully navigating regulatory hurdles, ensuring sufficient financing is in place, successfully concluding partnering discussions and, eventually, gaining commercial traction. COVID-19 has caused minimal disruption to the business; clinical trials were essentially complete and the key business functions can be performed remotely. The main sensitivities are detailed later (in the body of the note), with particular emphasis on the approval and commercialisation elements of the MED3000 programme.

Futura Medical: Rising to the challenges

Futura Medical is approaching a defining moment as it will shortly submit the first regulatory filing for MED3000, its topical gel for erectile dysfunction (ED). The remarkable results of the pivotal FM57 Phase III study have opened up new avenues: with a simpler and faster regulatory route to market, likely fresh patent protection, as well as new commercial options. MED3000's demonstrable clinical efficacy, coupled with a rapid onset of action and a clean side-effect profile, suggests that it is well placed to capture a sizeable share of a large, and growing, market. The subtleties that distinguish different ED patient segments and geographic markets mean that partnership discussions will not be straight-forward. We believe that more complex, targeted partnerships are required to maximise MED3000's value. Whilst not without risks, we feel the current valuation fails to reflect the likely future prospects.

MED3000 will shape the future, and the next 12 months are crucial

What a difference six months can make. Management is now actively progressing MED3000 for regulatory approval as a treatment for erectile dysfunction (ED). MED3000 consists of the specific DermaSys formulation that was used as the placebo arm in the pivotal FM57 Phase III study. A detailed analysis of the data shows remarkably consistent outcomes across all treatment groups and supports the view that MED3000 is an effective and safe therapy for all three forms of ED evaluated (Mild, Moderate, and Severe). The efficacy seen suggests an activity level close to that of the oral PDE5s such as tadalafil (Cialis), but with a faster onset of action (typically within 10 minutes) and fewer side-effects.

Positive regulatory interactions suggest timely approvals

Positive interactions with US and European regulators confirm that MED3000 meets the criteria for filing as a medical device, with the clinical package robust and essentially complete. It is likely that no further clinical work is required for Europe although a small study for the US may still be required. Paradoxically, the medical device route will likely result in faster approvals for MED3000 than originally envisaged for MED2005, which had glyceryl trinitrate (GTN) as the active drug. Provisionally, the data package for filing to the European Notified Body could be ready for end-July, with the FDA filing ready for submission during Q320, assuming that the next meeting with the FDA is equally productive,

An attractive profile in a large and growing market segment

The market opportunity for ED treatments is large, now worth c $5.6bn despite falling from its peak as genericisation of the leading PDE5 products takes hold. The number of men expected to seek treatment for mild- and moderate-erectile dysfunction is forecast to rise. We believe this is not simply because of increasing incidences due to demographics and the consequences of chronic diseases (such as diabetes), but also greater awareness and, importantly, expectations (from both partners) that healthy sexual activity can be restored. MED3000's profile, notably ease of use and rapid onset of action, coupled with eventual OTC status, suggests it offers material benefits that could capture a significant share of the ED market.

Inherent value is under-appreciated

Given the likely regulatory outcomes with MED3000, we believe the current valuation fails to reflect the future prospects and inherent value of the business. As discussed, our DCF model, based on modest assumptions, suggests a valuation of £153.8m, equivalent to 60.9p a share. We intend to revisit our model as progress is achieved and execution visibility improves.

A novel approach to erectile dysfunction (ED)

What a difference a pivotal Phase III trial result can make...

Six months ago we were expectantly awaiting data from the pivotal Phase III FM57 study of MED2005; a clear gel DermaSys formulation of the vasodilator glyceryl trinitrate (GTN) that is applied topically to the head of the penis (the glans). MED2005 had undergone an extensive development programme (c 15 clinical trials) to explore the best formulation, the pharmacokinetic profile, and dosage optimisation. The FM57 results, together with the planned FM59 Phase III trial, were the final elements and would support regulatory submissions in Europe and the US (most likely in early 2021). So, what has happened since?

Pivotal study demonstrates unexpected, yet clear, activity

FM57 consisted of three active arms, with GTN 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. Headline data (Exhibit 1) was announced in December 2019 (see Update notes) and showed a remarkably strong and consistent effect in all four arms, with clear and highly statistically significant improvements from baseline across Mild, Moderate, and Severe forms of ED. This striking lack of differentiation between any of the active arms and placebo would indicate that the action of the proprietary DermaSys formulation alone has an effect comparable to the GTN doses studied.

Exhibit 1: FM57 headline results – primary endpoints (change from baseline)

Primary Endpoints		MED3000	P-values	MED2005 0.6mg (0.2%)	P-values	MED2005 1.2mg (0.4%)	P-values	MED2005 1.8mg (0.6%)	P-values
IIEF-EF Domain	*Mean*	21.6	-	21.5	-	21.6	-	21.7	-
	*Change from Baseline LS Mean**	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)	*Mean*	86%	-	82.7%	-	85.5%	-	84.8%	-
	*Change from Baseline LS Mean ***	13.8%	<0.001	9.0%	<0.001	13.3%	<0.001	10.7%	<0.001
SEP3 (Did your erection last long enough for you to have successful intercourse)	*Mean*	58.6%	-	57.6%	-	59.1%	-	60.8%	-
	*Change from Baseline LS Mean***	23.2%	<0.001	20.8%	<0.001	22.6%	<0.001	23.3%	<0.001

Source: Futura Medical

Examination of data suggests the integrity of FM57 is sound

Whenever a well-structured clinical trial throws up such unexpected 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. Clearly the FM57 findings needed scrutiny and further detailed analysis of the data was performed. The individual results from each of the patient groups across some 60 centres (in nine countries) were examined and the methodologies of the two CROs (clinical research organisations) employed were investigated: the findings confirmed that the data are valid.

Primary endpoints are broad and clinically relevant

The primary efficacy endpoint for FM57 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 and adverse event profile.

Results are consistent across multiple measures and times…

The results for the primary endpoints (Exhibit 1 again) 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.

Exhibit 2: 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

…and across all grades of ED

Exhibit 2 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 ED 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 – 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

Exhibit 3 details the side-effect profile seen with the three MED2005 doses and the DermaSys placebo arm. Although the Exhibit's aim is 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 headaches findings in FM57. There is a clear dose response seen in the headache side-effect, a well-recognised problem with GTN administration, which again supports the view that the study was performed correctly. Interestingly, a similar, albeit smaller, 'placebo-effect' was seen in the four-week FM53 Phase II proof of concept study, although the hypothesis at the time was that the trial was not long enough to see clear separation between the active (0.2% GTN) and placebo (DermaSys) arms.

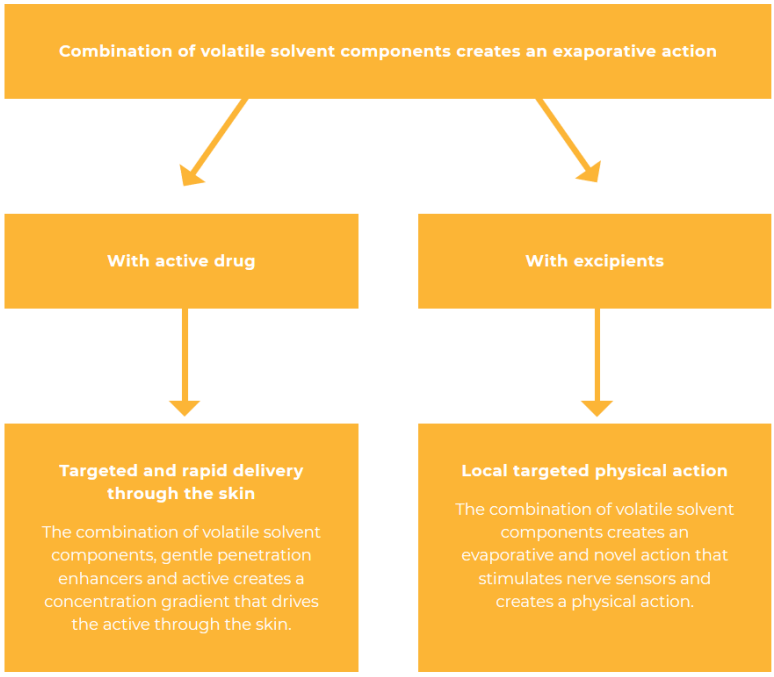
The collective body of evidence, notably from FM57 but also earlier work, taken in its entirety, indicates that this specific DermaSys formulation alone (now known as MED3000) is indeed a potent and effective treatment for all forms of ED.

How does MED3000 work as an erectogenic gel?

DermaSys technology drives absorption through the skin

The proposed mode of action of MED2005 was intuitively simple. A fast acting DermaSys formulation was selected to deliver glyceryl trinitrate (GTN), a well characterised vasodilator, topically to the head of the penis (the glans). The formulation was designed to provide a rapid transdermal delivery to the corpus cavernosum, where the required GTN concentration is achieved quickly and typically results in onset of erection within 5-10 minutes. The effect is local, with any systemic effects limited, and elimination from the body generally within an hour. The rationale, and elegance, of the approach made the results of FM57 all the harder to accept and yet the evidence appears compelling. So why does MED3000, the DermaSys formulation alone, work?

Exhibit 4: Mode of action of DermaSys transdermal technology



Source: Futura Medical Note: API = Active Pharmaceutical Ingredient

Evaporation and temperature swings appear to be the drivers

Exhibit 4 shows how evaporation is a key factor in how, with a typical pharmaceutical drug, the DermaSys transdermal delivery drives the penetration of an active ingredient through the skin. Essentially the selected formulation is

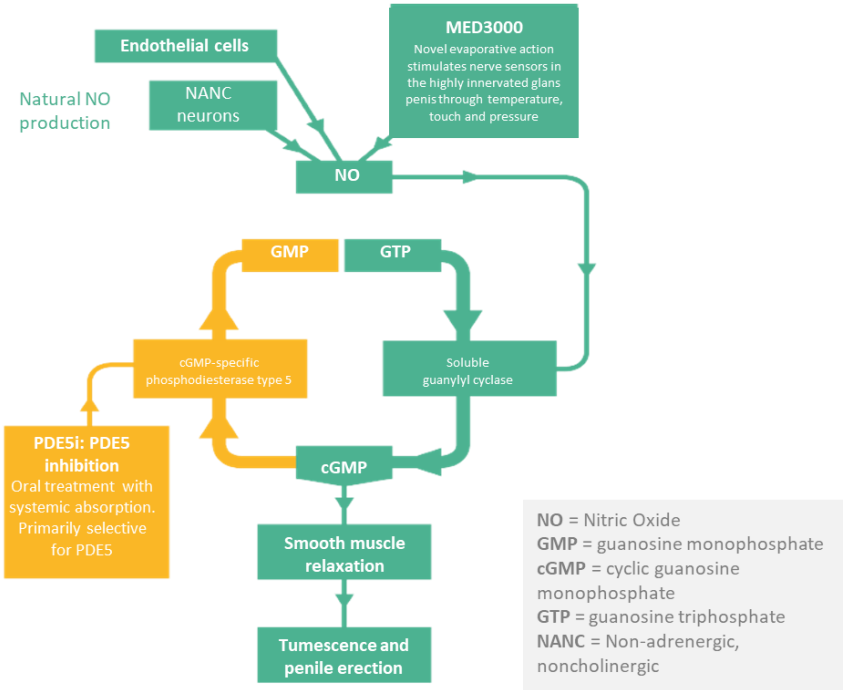
designed to be dynamically unstable when exposed to the air; this consists of a gel that contains volatile and non-volatile solvents. When applied topically the volatile elements evaporate very quickly and leave the remaining solvent supersaturated with active drug. This creates a high, and sustained, concentration gradient that pushes the active drug through the various layers of the skin to the site of action.

Mechanism possibly similar to cold-induced vasodilation

For MED3000 it appears that the effect arises from a combination of a first phase of marked, yet targeted, cooling within the first few minutes - a temperature change of up to 10°C has been measured - that happens as the volatile components of the DermaSys formulation evaporate rapidly. After this initial localised cooling, a second phase sees a sustained warming effect with the temperature recovering to slightly above the original temperature. As the glans area of the penis has many sensory nerve endings there is a surge of activity that appears to involve the endogenous NO pathways specifically.

The initial response to such a cooling would be a vasoconstriction, with reduced blood flows. However, the contrasting warming phase is then associated with a rebound vasodilation, that leads to relaxation of the smooth muscles and marked increase in local blood flows, with a resultant erection. Presumably the effect is comparable to the cold-induced vasodilation (CIVD) that occurs with extremities such as toes and fingers. Despite being a well-known effect, the mechanisms of CIVD are still disputed, but the pathways involved could well be similar. Interestingly, the precise mechanism of action does not need to be elucidated for the regulators to be comfortable for a product to be approved as medical device.

Exhibit 5: MED3000's mechanism of action



Source: Futura Medical

Positive interactions with regulators for approval

Encouraging feedback from both European and US medical device regulators

Futura Medical has engaged in fruitful discussions with both European and US regulators. The most significant being a pre-submission meeting with the FDA on

February 24, 2020, that supports the filing of MED3000 as a medical device for the treatment of erectile dysfunction. This would be a De Novo Classification, as there is no similar predicate device to allow a 510k submission, and would be examined on a clinical study report (CSR) based on the data generated by FM57 with additional clinical, safety, stability, and manufacturing information that is already being collated. The initial indications support the view that quality of the FM57 data may be acceptable without further pre-approval clinical studies.

Filings being prepared for first submission in Q320

A second pre-submission meeting to discuss the clinical sufficiency of FM57 and whether any post-marketing studies are required (a small one is likely in our view) is yet to be scheduled. Management expects this meeting to take place within a few months but is conscious that the current COVID-19 pandemic may affect timings. Assuming no unexpected events, this suggests that a filing could be ready for submission to the FDA by Q320.

We believe European OTC approval is likely

In Europe following similarly positive interactions with the designated EU Notified Body, the formal submission proceedings are now underway. The complete technical file, including the CSR and the Quality Management System data, should be complete ahead of planned submission by end-July 2020. It is worth noting that typically the default status for such medical device approvals could lead to MED3000's classification as an OTC product, unlike MED2005 which would likely have required an Rx-only interim stage prior to becoming available OTC.

US situation is more uncertain, yet still faster than MED2005

For our modelling we have assumed, conservatively given the COVID-19 uncertainties, that the review processes take a minimum of 12 months in both Europe and the US and so have approvals pencilled in for Q421. This is similar to our prior expectations for MED2005 Rx approval in Europe (see November 2019 Initiation report) but quicker than the 2024 timings we had pencilled in for an OTC switch. There is more uncertainty regarding MED3000's likely status in the US but, given its safety profile, there is a possibility that it could be quickly approved as an OTC product. This compares with our previous expectations that MED2005 would be approved as an Rx product in 2022, with a switch to OTC in 2025. The likely approval status currently remains uncertain and that is reflected in our valuation assumptions (see later).

ED is widespread and worth addressing

Erectile Dysfunction is not a trivial medical issue…

The importance of a healthy sexual lifestyle, for both men and women, was detailed in our Initiation, as was the nature and magnitude of ED as a clinical and social problem. All men will have experienced occasional episodes of loss of libido; however, the incidence and frequency tend to rise with age and the onset of certain diseases (notably diabetes and obesity). Importantly, it is not simply a modern "first-world" problem and nor is it a trivial inconvenience; an active sex life is associated with material improvements in mortality and quality of life measures.

…and it is increasingly common in an ageing society

ED, defined as the prolonged inability to attain and maintain an erection sufficient to permit satisfactory sexual performance, is a natural part of ageing. Hence, with an increasingly ageing population, nearly all men who live long enough are likely to develop ED. Studies have typically shown that in men aged 40 to 70, 48% had no dysfunction, 17% had minimal ED, 25% had moderate ED, and 10% had complete

ED. The more serious cases were often associated with metabolic conditions, such as diabetes, or cardiovascular conditions, such as atherosclerosis.

Viagra revolutionised the ED treatment landscape…

Approval of Pfizer's Viagra (sildenafil) in 1998 transformed the ED therapeutic landscape and brought it into the mainstream. Previously, treatments had centred on rather esoteric formulations of prostaglandin E1 (alprostadil) such as MUSE (Medical Urethral System for Erection), intra-urethral pellets (IUS), and Caverject, an intra-cavernosal injection (ICI), that increased blood flow into the penis. The pellet form results in a successful erection in 30%-40% of cases, while the injectable can achieve results in >80% of cases; although neither are easy to use.

…but older, and less discreet, options still remain popular

Other popular treatments included Vacuum Constriction Devices (VCD), essentially a clear plastic chamber that is placed over the penis and then a vacuum is created. If this results in a successful erection, a small constriction band is placed over the base of the penis to maintain an erection for around 30 minutes. The success rates of VCDs range from 50% to 80%. The cumbersome nature of these formulations and devices does mean a degree of planning is required, with a consequent loss of spontaneity and intimacy. Other options included surgery, with implantation of a penile prosthetic device, which have good long-term outcomes.

Two PDE5s brands became commercial titans

It was against this eclectic background that Viagra (sildenafil) burst into the clinical and public consciousness. The arrival of the PDE5 class transformed the ED marketplace. The availability of a simple oral medication resulted in a groundswell of patient awareness that was unheard of in pre-internet days. Viagra became a household name and doctors were soon asked for the product by brand name. The results were seen in the sales charts, with two of the original PDE5 products achieving blockbuster status (defined as annual sales over $1bn).

Differences between PDE5s are marginal; patient choice is key

Viagra was followed by the analogues Levitra (vardenafil, Bayer) and Cialis (tadalafil, Eli Lilly) in 2003. These differ mainly in their onset of action and duration of effect which, in the absence of properly conducted comparison studies, in reality means patient preference has become a primary determinant of choice. A fourth PDE5 inhibitor, Spedra/Stendra (avanafil), was launched in 2012 by Mitsubishi Tanabe, which claims to have the fastest onset of action (within 15 minutes). Other, mainly regional, "me-too" PDE5s are also available.

Exhibit 6: Top PDE5 inhibitors and key properties

	Generic (Brand)	Company	Median tmax (min)	Half-life (hours)	Absorption affected by food	Dosed
First generation	Sildenafil (Viagra)	Pfizer	60	3-5	Yes (high fat food)	As needed
	Tadalafil (Cialis)	Eli Lilly	120	17.5	No	Daily or weekender
	Vardenafil (Levitra)	Bayer	60	4-5	Yes (high fat food)	As needed
Second generation	Udenafil* (Zydena)	Dong-A Pharmaceutical	60-90	11-13	No	Daily or as needed
	Avanafil (Spedra/Stendra)	Menarini / Metuchen Pharma	30-45	5-10	No	As needed
	Mirodenafil* (Mvix)	SK Chemicals Life Science	75	2.5	Limited data	As needed

Source: Trinity Delta, Cleveland Clinic, FDA Note: * = not FDA approved

Viagra achieved peak sales of $2.1bn in 2012 (just ahead of patent expiries ex-US) and Cialis had peak sales of $2.3bn in 2017, whilst Levitra always ranked a poor third as its marketing campaigns failed to resonate with either users or clinicians, and it had no clear differentiation vs Viagra/Cialis. The newer "me-too" prescription PDE5s are not expected to achieve meaningful revenues as the market is effectively now genericised. However, the Viagra switch to OTC status in a number of markets means that established brand names have a renewed and longer lifecycle, albeit at a lower price point.

PDE5s have proven efficacy but still some notable limitations

Their commercial success reflects their clinical efficacy, with over two-thirds of men finding they provide sufficient improvement in their erections to achieve the desired intercourse. But, despite their undoubted benefits, PDE5s are not without their limitations[1]. Because of their mode of action, PDE5s are contraindicated in patients taking certain medications, notably nitrates and alpha-blockers, and between 11% and 18% of the mild and moderate ED population is excluded due to possibility of blood pressure interactions. A similar proportion, 12% to 16%, discontinue treatment due to side-effects (headaches, flushing, gastro-intestinal, and visual disturbances), despite these typically being transient and mild in nature. It is these interactions and side-effects that have, so far, created a barrier for many regulators to consider the switch to OTC.

Treatment discontinuations highlight the various issues

A larger proportion of ED patients, between 14% and 31%, discontinue treatment after an initial trial period, despite a satisfactory pharmacological effect. A recent meta-analysis suggests discontinuations over one year reach almost 50%[2]. The reasons vary by geography and age-group, ranging from a lack of desire and/or opportunity to a partner's loss of libido, and is probably related to individual cultural and psycho-social factors. However, a common theme (arising from both partners) is that the oral administration and need to "time it" means that there is a loss of spontaneity, and that intimacy and "naturalness" is reduced as a result.

MED3000 product characteristics offer benefits

An easy to use and effective transdermal gel applied directly to the tip of the penis

MED3000 is an elegantly simple clear gel formulation that is rapidly absorbed and results in a therapeutic effect within 5-10 minutes, faster than on-demand PDE5s. The patient benefits of MED3000 are summarised in Exhibit 7.

Exhibit 7: User benefits of MED3000

Benefit	Key enabling feature
Well tolerated	No systemic side-effect potential, especially compared to PDE5 inhibitors
Works rapidly	Potential to have one of the fastest speeds of onset (5-10 minutes) for any ED treatment
Enables spontaneity	Removes the need for planning of sex associated with some oral PDE5 inhibitor medications
Restores intimacy	Direct mode of application (by the male or his sexual partner) can form part of foreplay, which combined with speed of onset can help restore intimacy

Source: Trinity Delta, Futura Medical

[1] Phosphodiesterase-5 (PDE5) Inhibitors in the management of erectile dysfunction. Huang S et al Pharmacy & Therapeutics 2013 July 38(7):407, 414-419
[2] First generation phosphodiesterase type 5 inhibitors dropout: a comprehensive review and meta-analysis. Corona G et al. Andrology 2016, 4: 1002-1009

The rapid onset of effect, undoubted safety, and ease of use suggest MED3000 would offer an attractive, clearly differentiated (not 'me too'), and competitive clinical profile compared not only to the market leading class of PDE5 inhibitors, but other classes of competing ED therapies.

A sizeable opportunity with scope for growth

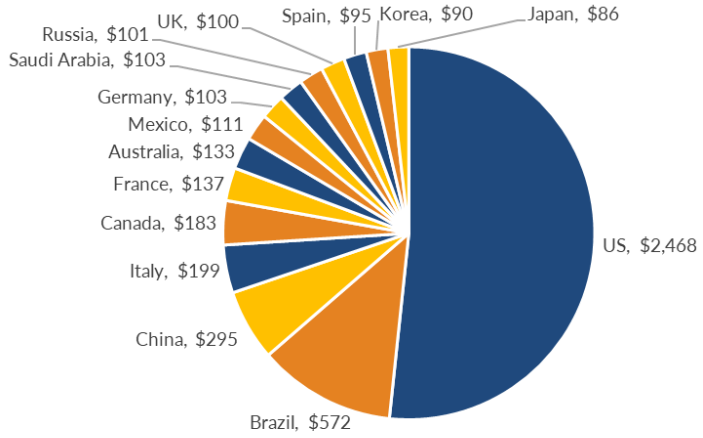
The ED market is large and growing across all geographies

The genericisation of the leading PDE5 brands, notably Viagra has resulted in the monetary value of the ED segment falling. This is seen when comparing the total sales for the ED category[3] in 2018 of $4.8bn, which was down from the 2017 peak of $5.8bn, as the patent expiries of the PDE5 class took their toll. The US, the largest value geography, saw the biggest decline with 2018 sales of $2.4bn, down from the 2017 result of $3.5bn. In contrast, volumes remain solid. In 2015 the global volumes[4] were 856m doses, growing by 4% CAGR to 958m in 2018.

Surprising difference in ED prevalence in US vs Europe

Estimates of ED prevalence vary according to the ages, health status, and emotional well-being of the study subjects; what emerges is that North America and areas in South East Asia typically have a higher prevalence than Europe and South America. For instance, MMAS showed the average prevalence in the 40-70 age group in the US is 52%, whereas in Europe[5] it is c 30%. Similarly, the incidence (the number of new cases) ranges from 19 to 66 per 1,000 men per annum, such that the current estimate of over 200m cases worldwide is forecast to rise to 322m cases by 2025[6].

Exhibit 8: The ED market sales by country 2018 ($m)



Source: IQIVA

The size of the ED population is not the addressable market

However, we would argue that this should not be considered as the addressable market for any ED treatment. Using the more comprehensive US sales data as a reality check, the 2018 ED volumes were 146.2m doses; which, using an average of 71 sexual episodes per annum in this age group, suggests some 2m men were

[3] IQVIA Midas Top 15 markets (formerly known as IMS Heath) data
[4] idem
[5] Age-related changes in general and sexual health in middle-aged and older men: European Male Ageing Study (EMAS). Corona G, et al. J Sex Med. 2010; 7:1362–1380.
[6] The worldwide prevalence and epidemiology of erectile dysfunction. McKinlay JB. Int J Impot Res. 2000;12 (suppl 4): S6-S11

routinely using a form of ED therapy. The result is highly dependent on the assumptions of the number of sexual episodes per annum, but even a conservative 12 per annum results in a population of around 12m. This compares with the around 30m US men which epidemiology studies predict as having ED.

Only a third of ED men will seek and then continue treatment

This is borne out by the clinical experience since Viagra was first launched twenty years ago, which, despite extensive and creative marketing campaigns, resulted in only around a third of men with mild-to-moderate ED actually seeking treatment. The reality is that, for a variety of factors, the majority of men will not do so; these probably reflect similar traits to those men mentioned earlier who discontinue PDE5 therapy and include decreased libido, absence of an interested sexual partner, medical contraindications, as well as embarrassment at admitting a need.

Probability of OTC status is the key variable in our view

MED3000 appears likely, in our view, to be approved as an OTC product relatively rapidly, most likely in Europe but possibly also in the US. Whilst it can be argued that an Rx indication can provide valuable professional validation to a patient, the greater availability and lack of embarrassment of an OTC indication should result in a materially faster adoption. The PDE5 OTC experience is increasingly demonstrating that sales volume growth is driven by the greater ease of access. Much clearly depends on the commercial partners, and their marketing and positional shrewdness, but even modest success results in large estimates.

We maintain a conservative approach in our modelling

Despite our deliberately conservative approach, we arrive at five-year sales for MED3000 of $225m in Europe and $250m in the US. Using more aggressive assumptions, notably on having motivated and commercially astute partners, could result in materially faster adoption curves and higher peak sales. Attempting to forecast likely Asian sales is thwarted by the number of variables and current lack of partnering visibility; hence these remain as pure upside to our modelling. Our estimates support the revenue expectations of $660m to $1bn that Futura Medical has collated from third-party agencies.

A direct OTC route would change partnership priorities

Addressing the emerging consumer health market needs new skills

In our Initiation we stated our view that there are no suitable global players that operate in the ED space, that are well positioned for both Rx (prescription only) and OTC, and for whom MED2005, and now MED3000, would be a strategically important product. The downsides of partnering with a dominant player, whose commercial priorities may alter over time, are well known to long-standing Futura Medical shareholders. Clearly, if MED3000 is rapidly approvable as an OTC product then partnering choices would be easier, but the basic premise remains.

We also referenced a recent White Paper by IQVIA, Consumer Health Innovation for the Future, that highlights how the OTC marketplace is evolving quickly and how the next wave of innovative products will require greater interaction between company, regulator, and patient. These developments are driven by an increasingly aware consumer, who has previously unimaginable access to healthcare information. These are seismic shifts in the marketplace, and such disruption inevitably means that the current leading players may not (and probably will not) remain the leaders in their fields.

Smaller, more nimble, regional specialists have great appeal in less conventional markets

We feel that the better partners would be smaller, nimbler, players for whom MED3000, and its success, would be a major element of their future growth. Partnership(s) with such players may also lend themselves to less traditional deal

types, such as a profit share or other novel deal structure. Greater risk-sharing would enable a deal to be structured to maximise income potential (especially in the key US market) at the expense of smaller upfronts. Additionally, we believe there are clear regional difference in how ED is perceived, and treatment sought. There are notable differences not only across major geographies such as Asia, Europe, and North America but also subtle, yet significant, variations between, for instance, Northern and Southern Europe.

Our view would be to appoint European (and Asian) partners then wait for the US

Our preferred option would be for any initial discussions to not be progressed until the details of the MED3000 approvals are known. The consumer, marketing, and even local legislation, differences across various geographies suggest that a single "global" partnership would not result in the optimal sales penetration over the longer term. Although logistically more complex, we would expect a series of regional partners being selected with, ideally, an element of profit share included.

Sensitivities

Key sensitivities are common to all small R&D driven companies

In common with most innovative healthcare companies the three main sensitivities relate to the clinical and regulatory aspects, the execution of the commercialisation plans, and the financial resources required to accomplish these. More specifically, the key near- and medium-term sensitivities are directed to the regulatory approvals and partnering progress of MED3000.

Increasing visibility on European and US regulatory pathways

The regulatory pathways for MED3000 in both Europe and US appear to be relatively clear, with submissions planned for Q3 and Q3/4 2020 respectively. The likely status, Rx initially versus OTC immediately, is still unclear but the probability of immediate OTC availability is, in our view, high. The status in the US is more uncertain but is, again in our view, more likely than not. We believe greater visibility is required before meaningful partnering discussions can advance.

New patent applied for, that could extend protection through to 2040

The patent position for MED3000 is probably more secure than that of MED2005, where its long development period resulted in a material erosion of the patent life, with the original formulation patent expected to expire in 2025 in Europe and 2028 for the US. A new patent application was filed in December 2019, which if granted, would protect MED3000 through to 2040. For our modelling we have applied a risk factor to allow for the uncertainty until feedback is received, which is likely within 6-12 months (COVID-19 impacts permitting).

Funding in place through to MED3000 approvals

Funding is an ever-present issue for pre-revenue healthcare companies and Futura Medical is no exception. The tight focus on cost control has meant that the R&D spend has been modest and the clinical programmes to date achieved with commendable thrift. In part this reflects the "virtual" company structure, with only 15 employees and the remainder of the workflows outsourced as necessary. Funding requirements for the European filings is likely to be modest; the US filings may require some additional clinical data, with the final requirements expected to be known by early-Q320. Cash of £2.51m at end-December 2019 was bolstered by the proceeds of the £3.25m (gross) equity raise received in January 2020 and the £2.22m of R&D Tax credits expected in mid-2020.

When, where, and what is the best out-licensing strategy?

The key question remains as to what the best value-creating out-licensing strategy for MED3000 is? We believe that an early and wide-ranging deal is unlikely to achieve the optimal outcome. As stated previously, selecting appropriate partners for the differing geographies (with their individual needs) is, in our view, preferable to a global deal. Similarly, we would prefer smaller upfront payments and a larger royalty on sales element. And finally, an element of risk sharing would not be something that we would criticize, especially for the commercially important US market.

COVID-19 appears to have caused minimal disruption

COVID-19 has impacted all businesses to some extent. Within the healthcare industry, the largest effect has been on the timelines for starting and enrolling clinical trials (notably first-in-man studies that typically require access to ITUs). Futura Medical currently has no clinical trials in place, being principally focussed on preparing regulatory submissions for MED3000. The virtual model means that the company has transitioned to remote working seamlessly, with minimal disturbance to its operations.

Valuation

Risk-adjusted DCF model is the best valuation tool

We use a DCF model to value Futura Medical. The key value driver is MED3000 and we examine its sales potential and launch timings in the US and European markets. We assume that MED3000 has a high likelihood of being approved as an OTC medical device in Europe in the near-term, whereas in the commercially important US market we have been more cautious with our success probabilities. As before, we exclude any contribution from potential Asian market sales until the commercialisation pathway is more visible.

Assumed an income stream equivalent to a 20% royalty rate

We have assumed that Futura Medical receives payments from partners that are equivalent to a royalty rate of 20%, although in reality they will likely be a combination of small upfront payments, sales milestones, and tiered royalties on sales. The risk adjustments used reflect the remaining regulatory risks and the inherent commercial and execution sensitivities for each market. These are summed and netted against the costs of running the operation and net cash.

Valuation of £153.8m, or 60.9p per share (fully diluted)

We have also updated our model (Exhibit 9) for the recent fund raise (both net cash and the number of shares outstanding). There are multiple variables that affect the outcome of the valuation, with the key ones being the likelihood of regulatory approvals, the length of patent life, and competence and expertise of the commercialisation partners. Our current valuation for Futura Medical is now £153.8m, or 60.9p per share on a fully diluted basis, compared with £127.5m (62.4p per share) previously.

Exhibit 9: Futura Medical risk-adjusted DCF model

	Total NPV ($m)	Total NPV (£m)	Risk adjustments	rNPV ($m)	rNPV (£m)	rNPV/ share (p)	Notes
MED3000 (Europe)	165.2	127.1	63%	104.1	80.0	31.7	Peak sales: $225m Launch year: 2022
MED3000 (US)	181.3	139.4	54%	97.9	75.3	29.8	Peak sales: $250m Launch year: 2022
TPR100	2.3	1.7	40%	0.9	0.7	0.3	Peak sales: $6.2m Launch year: 2022
Non-R&D opex	(4.4)	(3.4)		(4.4)	(3.4)	(1.3)	
Net cash	1.5	1.2		1.5	1.2	0.5	At H120e
Total	**345.9**	**266.0**		**200.0**	**153.8**	**60.9**	

Source: Trinity Delta Note: Assumptions include a 12.5% discount rate; a 1.3 $/£ FX rate, and 10% tax rate from 2026 with the benefit of the UK patent box

MED3000 will likely be launched first in Europe…

For Europe, we have assumed that the first launch, initially as an Rx indication but with a possibly rapid switch to an OTC product, is in 2022, with peak sales of $225m occurring around five years post-launch. The rNPV for Europe is £80.0m ($104.1m), equivalent to 31.7p per share.

…but US has the potential to be more sizeable in the longer term

For the US market we also assume launch in 2022, with peak sales of $250m. We have modelled an OTC availability two years from approval and flexed the success probability to allow for the current degree of uncertainty. It is here that the greatest sensitivity in our valuation lies. However, if the US market does continue to evolve towards there being less of a demarcation between Rx and OTC in the commercialisation of "lifestyle" drugs, then not only will the differences between Rx and OTC status diminish but access to (and in turn, adoption of) such drugs

would improve too. Our total rNPV for the US is £75.3m ($97.9m) or 29.8p per share. As this is an important element in our modelling, we will revisit as there is more clarity around future market developments.

In both cases we have been conservative with the patient numbers, addressable market, marketing and promotional campaigns, and adoption curves. We prefer to be cautious in our approach and intend on reviewing our models once the likely partners, and possible terms, for commercialisation are known.

TRP100 adds a relatively minor £0.6m, or 0.3p per share

The TPR100 programme, with Thornton & Ross (part of STADA AG), accounts for little in our model and essentially it is only included for completeness. Our valuation is based on first approval and launch in 2023 in the UK only. We will include the contributions from additional regions once they are partnered. We assume peak sales of £6.2m, with an rNPV of £0.7m ($0.9m) or 0.3p per share. Similarly, for completeness, the early stage of the cannabinoid programme, CBD100, with CBDerma Technology means is it not yet included in our model. In both cases we would revisit our assumptions as visibility on progress improves.

Summing these and netting out the costs of the running the business and cash gives our risk-adjusted valuation of £158.8m, equivalent to 60.9p a share.

Financials

Net loss is contained as emphasis is on cost control…

Futura Medical reported FY19 results that showed tight control which limited the net loss to £8.92m, up from £5.88m. The increase was due to the rise in R&D spend (FY19: £10.05m vs FY18: £6.03m) reflecting the cost of the FM57 Phase III study, that was completed on time and on budget. Admin costs of £1.14m, down from £1.23m in FY18, reflect the efforts to maintain a lean central team. The R&D tax credit was £2.2m, up from £1.3m, again reflecting higher R&D spend in the period. Payment of the refund typically happens mid-year but may be impacted by issues associated with COVID-19.

…and cash resources suggest a comfortable runway

Cash of £2.51m at end December 2019 (£9.16m at end-FY18) was subsequently bolstered by a £3.25m (gross) fund raise in January 2020. Costs associated with FM57 increased FY19 cash burn to £8.01m (up from £5.63m in FY18). FY20 burn is expected to be materially lower, with only limited spend on closing out the FM57 data and preparation for the US and European regulatory filings. Assuming no major clinical work is required to support MED3000 filings, existing resources and expected R&D tax credit receipt means that Futura' Medical's cash runway is expected to last through to Q221.

Regulatory filings set to become the biggest cost item

Looking ahead, we expect R&D investment to reduce materially. Expenditure in the other disclosed development programmes is small and essentially financed by partners, with similar funding arrangements expected for any future projects. Costs associated with the regulatory filings of MED3000 in the various regions is expected to be the largest single element of spend. Admin expenses should remain contained as the small central team is highly cost effective (only 15 staff are employed directly, the remaining workload is largely outsourced and varies as programmes progress). We estimate that Futura Medical's low-cost strategy means that recurring underlying costs will remain around £2.5m a year.

Multiple options to address longer term funding

In the longer term, it could be argued that sufficient funding would arise from the upfront payments of any out-licensing and partnering deals. Whilst this is possible, we would expect such deals to be structured to maximise the overall income potential (especially in the important US market), which suggests greater risk-sharing and smaller (if any) upfronts. An appeal of the risk-sharing route is that, in our view, Futura Medical is well placed to find funding if required from a variety of possible sources, including debt instruments, equity, or a hybrid combination.

Exhibit 10: Summary of financials

Year-end: December 31 £'000s	2017	2018	2019	2020E	2021E
INCOME STATEMENT					
Revenues	**363**	**0**	**32**	**0**	**0**
Cost of goods sold	0	0	0	0	0
Gross Profit	**363**	**0**	**32**	**0**	**0**
R&D expenses	(4,100)	(6,039)	(10,051)	(3,554)	(2,575)
General and administrative expenses	(1,118)	(1,228)	(1,144)	(1,238)	(1,312)
Underlying operating profit	**(4,856)**	**(7,266)**	**(11,164)**	**(4,792)**	**(3,887)**
Other revenue/expenses	0	0	0	0	0
EBITDA	**(4,843)**	**(7,247)**	**(11,143)**	**(4,774)**	**(3,873)**
Operating Profit	**(4,856)**	**(7,266)**	**(11,164)**	**(4,792)**	**(3,887)**
Interest expense	19	28	22	4	5
Profit Before Taxes	**(4,837)**	**(7,239)**	**(11,141)**	**(4,788)**	**(3,882)**
Adj. PBT	**(4,837)**	**(7,239)**	**(11,141)**	**(4,788)**	**(3,882)**
Current tax income	936	1,358	2,222	809	592
Cumulative preferred stock dividend	0	0	0	0	0
Net Income	**(3,900)**	**(5,881)**	**(8,919)**	**(3,979)**	**(3,290)**
EPS (p)	**(3.2)**	**(4.5)**	**(4.4)**	**(1.6)**	**(1.3)**
Adj. EPS (p)	**(3.2)**	**(4.5)**	**(4.4)**	**(1.6)**	**(1.3)**
DPS (p)	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
Average no. of shares (m)	120.6	131.9	204.7	242.2	245.6
Gross margin	*100%*	*N/A*	*100%*	*N/A*	*N/A*
BALANCE SHEET					
Current assets	**9,541**	**10,830**	**4,842**	**1,965**	**3,794**
Cash and cash equivalents	8,363	9,158	2,511	1,048	3,093
Accounts receivable	181	306	101	101	101
Inventories	70	8	8	8	8
Other current assets	927	1,358	2,222	809	592
Non-current assets	**64**	**47**	**60**	**49**	**42**
Property, plant & equipment	64	47	60	49	42
Other non-current assets	0	0	0	0	0
Current liabilities	**(499)**	**(2,026)**	**(4,848)**	**(2,909)**	**(7,909)**
Short-term debt	0	0	0	0	(5,000)
Accounts payable	(499)	(2,026)	(4,848)	(2,909)	(2,909)
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**	**54**	**(894)**	**(4,072)**
Share capital	44,913	50,393	50,412	53,337	53,337
Other	(35,807)	(41,541)	(50,359)	(54,231)	(57,409)
CASH FLOW STATEMENTS					
Operating cash flow	**(4,155)**	**(4,680)**	**(6,634)**	**(4,381)**	**(2,947)**
Profit before tax	(4,837)	(7,239)	(11,141)	(4,788)	(3,882)
Non-cash adjustments	195	140	100	120	121
Change in working capital	(385)	1,464	3,027	(1,939)	0
Interest paid	19	28	22	4	5
Taxes paid	851	927	1,358	2,222	809
Investing cash flow	**(56)**	**(5)**	**(33)**	**(7)**	**(8)**
CAPEX on tangible assets	(56)	(5)	(33)	(7)	(8)
Other investing cash flows	0	0	0	0	0
Financing cash flow	**221**	**5,480**	**19**	**2,925**	**5,000**
Proceeds from equity	221	5,480	19	2,925	0
Increase in loans	0	0	0	0	5,000
Other financing cash flow	0	0	0	0	0
Net increase in cash	**(3,990)**	**795**	**(6,647)**	**(1,463)**	**2,045**
Cash at start of year	12,353	8,363	9,158	2,510	1,048
Cash at end of year	**8,363**	**9,158**	**2,510**	**1,048**	**3,093**
Net cash at end of year	**8,363**	**9,158**	**2,511**	**1,048**	**(1,907)**

Source: Company, Trinity Delta Note: Adjusted numbers exclude exceptionals. The funding requirement is shown as short-term debt in FY21e, until transaction type, source and size are confirmed.

Company information

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Key personnel

Person	Position	Biography
John Clarke	Non-Executive Chairman	Chairman since 2012, following a 35-yr career at GlaxoSmithKline latterly as President of GSK Consumer Healthcare (2006 to retirement, 2011). Non-Exec Chairman of Science in Sport, Kind Consumer and, pre-acquisition, Quantum Pharma. A senior adviser to Helios Investment Partners LLP.
James Barder	CEO	CEO since 2001. Previously Managing Director of Aon Capital Markets and Non-Exec Director of Lorega Ltd. Extensive experience in striking and managing partnerships and licensing agreements.
Angela Hildreth	FD and COO	Joined in 2018, adding further financial, operational, and strategic experience to the executive team. Previously six years as UK Finance Director at Shield Therapeutics Plc.
Ken James	Head of R&D	Joined in 2016. Previously SVP of R&D for GSK Consumer Healthcare, having spent over 40 years in a variety of roles there and bringing over 200 consumer products to market.

Top shareholders

	% holding
Lombard Odier Asset Management (Europe) Ltd	21.04
T Adams	8.08
WT Lamb Investments Ltd	5.23
RA Lamb	3.71
Disclosable shareholdings (>3%)	**38.06**
Other shareholders	61.94
Total shareholders	**100.00**

Source: Futura Medical

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Disclaimer

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