TheraCryf

Initiation – strong healing

20 May 2024

Price
0.75p

TICKER
TCF

Market Cap
£3.2m

Net cash (30 April 2024)
c£3m

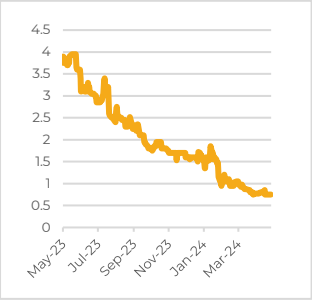
Free Float
100%

3mo Av. Daily Volume
1.4m

Broker
Cavendish

Index
AIM

Share Price Performance



Source: Bloomberg

TheraCryf is a clinical stage drug development company working to commercialise its proprietary formulation of sulforaphane, SFX-01, and its expanded portfolio of drug development candidates, following the recent acquisition of Chronos. The company's focus is on cancer, neurodevelopmental disorder, and neuropsychiatric drugs. Potential target markets total in the billions of dollars. The company is financed through toward the end of FY26.

Colin Smith
+44 20 7082 5522
Email the Analyst

Drug developer focused on cancer and behavioural brain disorders

TheraCryf is a clinical stage drug development company focused on commercialising its proprietary formulation of sulforaphane, SFX-01, and two novel drug candidates acquired in the recent Chronos transaction. The primary targets for SFX-01 are cancer and neurodevelopmental disorders while TheraCryf's new orexin and DAT programmes, extend the company's reach into neuropsychiatric drugs, currently a very active area for acquisitions and partnering. Potential target markets total in the billions of dollars. The company has multiple academic collaborations and a partnership with Stalicla potentially worth up to US$161m in milestone payments. The company has a financial runway through towards the end of FY26. Despite its advantages, TheraCryf trades on a fraction of the rating of peers with similar characteristics and has multiple prospective newsflow events due in 2024/25.

Sulforaphane is created naturally on the consumption of broccoli and other cruciferous vegetables but is very unstable in its natural form. TheraCryf has a patented core technology, Sulforadex®, for the production of a fully synthetic, clinical grade sulforaphane (SFX-01) in tablet form which is not to be confused with any niche dietary supplement based on botanical extracts.

Sulforaphane has demonstrated action on three distinct disease-relevant cellular pathways and interest in sulforaphane as a clinical therapy is high. That has enabled TheraCryf to enter into multiple academic collaborations and into a partnership with Stalicla which sees it fund the development of SFX-01 into Phase 2 clinical trials for the treatment of autism spectrum disorder.

The Chronos acquisition has added an orexin programme and a dopamine transporter (DAT) inhibitor programme to TheraCryf's drug development portfolio. While these programmes are at the pre-clinical stage, they have shown highly promising results during *in vivo* testing in animal models and have large potential markets. TheraCryf is now seeking non-dilutive funding to advance these programmes with a priority to the orexin programme for which the target is Binge Eating Disorder, a condition more common than anorexia and bulimia combined.

Following peak expenditure in FY23, TheraCryf is aggressively managing its expenditure which, together with the recent net £0.8m equity raise, should allow the company to extend its cash runway through towards the end of FY26, we expect.

Despite its advantages, the market appears to be disproportionately pessimistic about TheraCryf's chances of success. As against eleven peers, TheraCryf has the lowest market capitalisation of the group at just £3m, yet it is potentially due substantial milestone payments to which it trades on by far the least demanding multiples. Moreover, it is one of only six of the group with active ongoing clinical trials and its lead candidate is targeting large, rather than niche markets while it has multiple share-price significant points of newsflow due in 2024/25.

At a Glance (Yr. to Mar)	Revenue (£k)	Opex (£k)	Net profit/ (loss) (£k)	Dil EPS (p)	Net (cash)/ debt (£k)*
FY22A	0	(3,193)	(2,730)	(0.99)	(9,030)
FY23A	442	(5,546)	(4,043)	(1.47)	(5,000)
FY24E	400	(4,026)	(3,089)	(1.12)	(2,022)
FY25E	0	(2,026)	(1,682)	(0.39)	(1,384)
FY26E	0	(2,026)	(1,682)	(0.39)	138

*Source: TheraCryf, CAG Research. *Excludes any milestone payment.*

Contents

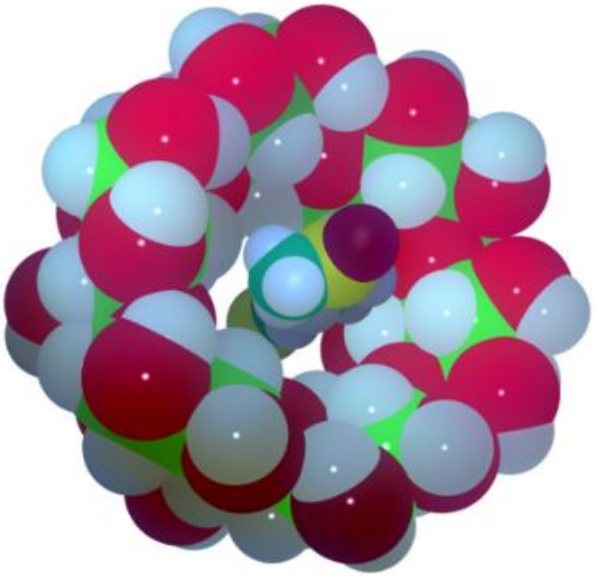
Investment thesis

TheraCryf is a clinical stage drug development company focused on commercialising its proprietary formulation of sulforaphane, SFX-01, and two novel drug candidates acquired in the recent Chronos transaction. The primary targets for SFX-01 are brain cancer and neurodevelopmental disorders while the acquisition extends TheraCryf's portfolio into neuropsychiatric drugs, currently a very active area for acquisition and partnering. TheraCryf's strategy is to leverage third party funding, once drug development is sufficiently advanced, and it has multiple academic collaborations and a partnership with Stalicla under which TheraCryf is due potential milestone payments of up to US$161m. TheraCryf tripled its drug development pipeline with the Chronos acquisition and now has a cash runway through towards the end of FY26. Despite its advantages, TheraCryf trades on a fraction of the rating of peers with similar characteristics and has multiple prospective upcoming newsflow events.

TheraCryf is an AIM listed clinical stage drug development company. With the recent acquisition of Chronos Therapeutics (Chronos), TheraCryf, formerly known as Evgen, tripled its pipeline of promising drug development candidates. These include its proprietary formulation of synthetic sulforaphane, SFX-01, (see Synthetic sulforaphane) which has undergone successful initial clinical trials, and two late stage, pre-clinical compounds, an orexin 1 antagonist (see Orexin programme), initially targeted for use in the treatment of Binge Eating Disorder (BED), and a DAT inhibitor (see DAT programme), initially targeted for use in the treatment of fatigue in patients suffering from multiple sclerosis. The total addressable market for these compounds and/or their derivatives is in the billions of dollars.

Sulforaphane is a highly active compound showing significant potency in clinical trials for the treatment of multiple diseases, including cancer. However, in its natural form, sulforaphane is highly unstable. TheraCryf's key distinction is that it has patented technology (Sulforadex®) for synthesising sulforaphane into an active, stable, and solid pharmaceutical grade material. SFX-01 (Figure 1) made using TheraCryf's Sulforadex® technology is the company's most advanced clinical asset.

Figure 1: SFX-01 molecule



Source: TheraCryf, CAG Research.

SFX-01 is the only pure form of sulforaphane that can be administered as a pharmaceutical and is not to be confused with any niche dietary supplement based on botanical extracts.

The objective of TheraCryf's sulforaphane programme is to establish a dominant position in the development of pharmaceuticals based on sulforaphane and related analogues, thereby meeting unmet clinical need, and improving patient outcomes.

The orexin programme, acquired as part of the recent Chronos acquisition, comprises an orexin 1 antagonist with the potential to treat addictive disorders, initially targeting BED. The DAT programme comprises a dopamine transporter inhibitor, initially targeting the fatigue widely experienced by patients suffering from multiple sclerosis.

Both the orexin and the DAT programmes are at the pre-clinical stage but have shown highly promising results during *in vivo* testing in animal models and have large potential markets.

The addition of the orexin and DAT neuropsychiatry assets are complementary to the neurodevelopmental disorders and brain cancer which are the current active target of the development of SFX-01.

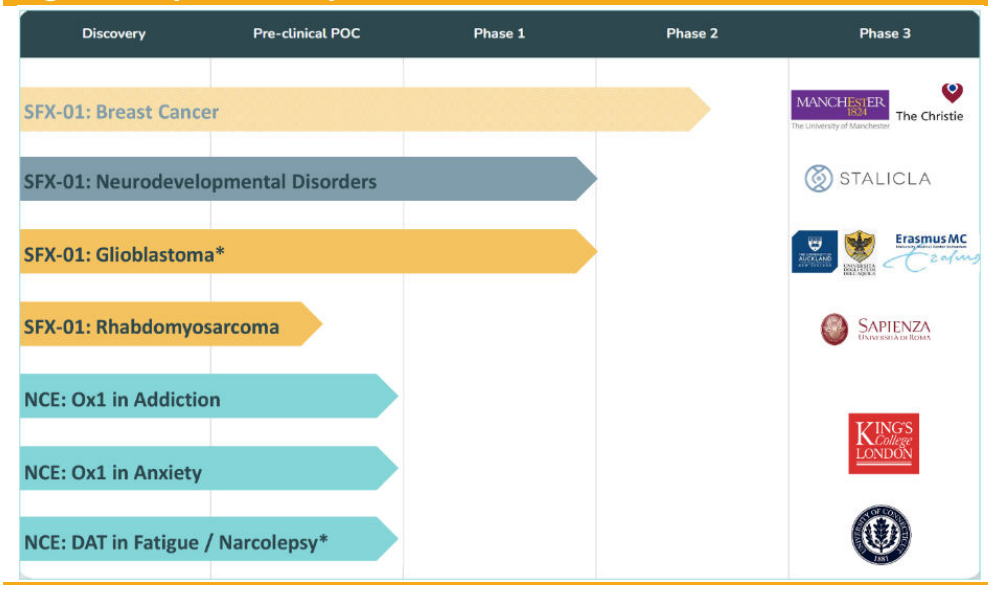
TheraCryf's business model is to develop its assets up to compelling datasets no later than clinical Phase II study proof of concept and then licence them out to larger pharmaceutical companies able to commercialise them. In the short to medium term, the company is focused on the application of SFX-01 in cancers and neurodevelopmental diseases and advancing its orexin programme, most likely on a grant funded basis while remaining open to opportunistic partnerships where there is a convincing scientific and commercial rationale. Given the company's focus on shareholder returns, it is open to realising any of its development programmes at an attractive valuation.

The company's strategy is to leverage third-party funding available to academics and from biopharma companies in order to generate pre-clinical and clinical data at a low rate of cash burn to itself. Unusually for a company of this type, it is now funded through towards the end of FY26, following the equity raise completed in April.

Last August, TheraCryf reported successful completion of a Phase 1b healthy volunteer study using its new enteric coated tablet formulation of SFX-01 which is able to pass through the stomach without damage and releases sulforaphane in the gut where it is taken up by the body. The study demonstrated that after dosing, sulforaphane and its metabolites were present in the blood at clinically effective concentrations equivalent to those seen during both *in vitro* and *in vivo* testing without resulting in any serious adverse events to the volunteers on test. Additional pharmacodynamic exploratory investigation showed changes in gene expression after dosing with SFX-01 even in healthy volunteers, confirming the pharmacological impact of SFX-01 on those given the drug.

TheraCryf's expanded clinical pipeline covers seven areas of development ranging from discovery through pre-clinical proof of concept to Phase II test readiness (Figure 2) with nine different partners (see Partnerships and collaborations).

Figure 2: Pipeline and partners



Source: TheraCryf, CAG Research.

Currently the most active components of the pipeline are the licence agreement with Stalicla, the Glioblastoma study with Erasmus University, and the collaboration with University La Sapienza di Roma investigating the potential for SFX-01 to enhance the effectiveness of radiotherapy in the treatment of Rhabdomyosarcoma. In addition, TheraCryf has commenced a collaboration with the University of Michigan for the use of SFX-01 to prevent colorectal cancer. Further developments in any of these lines together with any potential new partnerships could trigger a significant share price response, particularly considering the £3m market capitalisation of TheraCryf and these should also result in multiple newsflow events through 2025 (Figure 3).

Figure 3: Potential newsflow 2024/25

Partner/collaborator	Indication/Area	Newsflow
Erasmus U.	Glioblastoma	Results of pre-clinical work
Stalicla	ASD[1]	Launch of P2 clinical trial
Stalicla	ASD[1]	FDA grant of IND[2] status
U. Sapienza	Rhabdomyosarcoma	Radiosensitisation data
U. Michigan	Colorectal cancer	Initial *in-vivo* results
TheraCryf	SFX-01 healthy volunteer study	P1b scientific publication
Kings College London[3]	Orexin programme	Grant funding

Source: TheraCryf, CAG Research. 1) Autism Spectrum Disorder; 2) Investigational New Drug; 3) Potential/other suitable partner.

As there are no current commercial sales of SFX-01 for therapeutic use, TheraCryf's revenue is intermittent, reflecting milestone and initial license payments. The group expects to incur losses for the foreseeable future. The company's R&D effort generates a steady stream of cash tax receipts which have averaged c£0.5m pa over the last five years which typically cover around 14% of the cost base. Tax receipts for FY24 will reflect the high level of eligible spend in FY23 with £0.9m reported as being received at the interim stage.

Following the peak level of expenditure in FY23, costs are set to fall c30% in FY24 and we expect tight cost control to result in a further c50% YoY reduction in costs prospectively as the company focuses on extending its cash runway through towards the end of FY26.

The company acquired Chronos in April 2024 for a total initial consideration of £0.9m satisfied by the issuance of 62.3m consideration shares priced at 1.44p/share. In conjunction with the Chronos deal, TheraCryf raised net £0.8m in equity funding which, together with pre-existing cash and net cash of £2.0m, gives the company a net cash position of around £3m, we calculate.

On our estimates, TheraCryf will extend its cash runway through towards the end of FY26 excluding any additional milestone payments which may be paid or any non-dilutive funding which may be generated by the company for the further development of its drug development pipeline (Figure 4).

Figure 4: Key financials (£k)

Item (March YE)	FY22A	FY23A	FY24E	FY25E	FY26E
Revenue	0	442	400	0	0
Operating expenses	(3,193)	(5,546)	(4,026)	(2,026)	(2,026)
Tax repayment	533	475	913	462	344
Tax repayment as % of opex	17%	9%	23%	23%	17%
Net loss	(2,730)	(4,043)	(3,089)	(1,682)	(1,682)
Diluted EPS	(0.99p)	(1.47p)	(1.12p)	(0.39p)	(0.39p)
Net (cash)/debt	(9,030)	(5,000)	(2,022)	(1,384)	138

Source: TheraCryf, CAG Research.

Should sulforaphane eventually be approved for clinical use, the total markets it is targeting are scaled in the multiple-billions of dollars while TheraCryf's pre-clinical programmes also target large markets. At TheraCryf's current stage of development we believe it is too speculative to build DCF based models of potential use values to derive a point valuation. However, we can demonstrate that markets appear to be disproportionately pessimistic about the risks TheraCryf faces in achieving significant commercial value compared to other valuations in the market.

Figure 5 lists all companies with a primary listing in the UK, a market capitalisation of under £100m, and whose primary business is drug development.

Figure 5: TheraCryf valuation to peers

Company	Mkt cap (£m)	Disclosed max milestone (US$m)	Disclosed milestone /mkt cap (X)	Disclosed milestone /EV (X)	Sales (£m)	Most advanced current trial	Net cash /(debt) (£m)	Focus
TheraCryf	3.2	161	40.2	312.9	0.4	Phase 1	3.0	Cancer, neurodevelopmental disorder, neuroscience
Scancell	91.6	624	5.4	5.0	5.3	Phase 2	-5.9	Cancer and infectious diseases
Redx Pharma	58.3	755	10.4	14.8	4.2	Phase 2	18.1	Fibrotic disease and cancer
Arecor Therapeutics	41.8	n/d	n/a	n/a	2.4	Phase 1	8.2	Diabetes; reformulating existing therapies using Arestat™ platform
Hemogenyx Pharma	20.6	n/a	n/a	n/a	0.0	Pre-clinical	1.2	Blood disease
Destiny Pharma	16.4	570	27.7	44.7	0.0	Phase 3	6.4	Infection prevention
Synairgen	11.8	n/a	n/a	n/a	0.0	n/a	14.6	Viral lung infection
Bivictrix Theapeutics	9.5	n/a	n/a	n/a	0.0	Pre-clinical	1.9	Cancer
Immupharma	9.2	n/d	n/a	n/a	0.0	Phase 2/3	0.2	Autoimmunity & inflammation; anti-infection
Genflow Bioscience	6.5	n/a	n/a	n/a	0.0	Pre-clinical	0.7	Liver, Werner Syndrome
Roquefort Therapeutics	5.9	n/a	n/a	n/a	0.0	Pre-clinical	0.5	Cancer
ValiRx	4.1	20	3.9	5.0	0.0	n/a	0.9	Cancer, women's health

Source: Companies, CAG Research.

Of the dozen companies listed in Figure 5, TheraCryf has the lowest market capitalisation of the group at just £3m and the second lowest EV, yet it is potentially due substantial milestone payments to which it trades on by far the least demanding multiples. Moreover, it is one of only six of the group with active ongoing clinical trials and its lead candidate is targeting large, rather than niche markets.

In our view, Figure 5 demonstrates that TheraCryf, despite having the characteristics common to the most valuable companies in the table, trades on the lowest market capitalisation and one that is less than many companies with no drug in trial and no drug sufficiently advanced to persuade drug developers to enter into out-licensing agreements. Moreover, given the number of investigations and trials that TheraCryf has in train, there should be multiple points of newsflow in 2024/25 (Figure 3), each of which could have a significant impact on the share price.

The addition of the Chronos portfolio of neuroscience assets (see Orexin programme and DAT programme) trebles the number of clinical assets in TheraCryf's portfolio. Both programmes address large potential markets and are in what is currently a very hot area for drug development.

Since the start of 2023 the total value of out-licensing deals, acquisitions and funding transactions in the area of neuroscience exceeds US$23bn and includes some of the largest names in big pharma as well as a host of biotech drug developers (Figure 6).

Figure 6: Neuroscience related transactions

Subject	Target/Funding	Value US$m	Date	Neuroscience target
Pharmanovia	Asxome Therapeutics	167	Feb-23	Sunosi/excessive daytime sleepiness
AstraZeneca	Orexin/AXD4041	n/a	Nov-23	Opiod use disorder, Phase 1 trial
Invidior	C4XD/Orexin	20	Aug-23	Orexin-1 receptor antagonist, C4X_3256
Johnson&Johnson	n/a	n/a	Dec-23	Neuroscience one of four focus areas in Innovative Medicine
AbbVie	Cereval Therapeutics	8.7bn	Dec-23	Various inc schizophrenia, Parkinsons, & mood disorders
Bristol Myers Squibb	Karuna Therapeutics	14.0bn	Dec-23	Schizophrenia
Neurona Therapeutics	Series E financing	120	Feb-24	Epilepsy
Engrail Therapeutics	Series B financing	157	Mar-24	Anxiety disorders, depression, PTSD
Neurosterix	Company launch	63	Apr-24	Allosteric modulators
Seaport Therapeutics	Series A financing	100	Apr-24	Neuropsychiatric medicines/Glyph platform
Reunion Neuroscience	Series A financing	103	May-24	Postpartum depression

Source: Companies, CAG Research.

TheraCryf is now actively seeking non-dilutive funding to advance the drug development pipeline acquired with Chronos with a focus on the orexin programme.

Purpose, opportunity, and strategy

TheraCryf's purpose is to build a drug development business in oncology and behavioural brain disorders, commercialising its newly expanded drug development pipeline, thereby benefitting patients and shareholders. Given the range of possible therapeutic uses, the potential overall markets for the company's existing pipeline of assets is in the multiple-billions of dollars. TheraCryf's primary strategy is to leverage third-party funding to develop drugs up to Phase II proof of concept trials with a view to out-licencing to drug development companies able to carry them through to commercialisation.

TheraCryf's lead asset is sulforaphane which is in the clinical stage while the recent acquisition of Chronos added assets in the late pre-clinical stage the most important of which are an orexin programme involving an orexin 1 receptor antagonist and a dopamine transporter inhibitor (DAT) programme.

The sulforaphane opportunity is derived from TheraCryf's unique ability to synthesise pure sulforaphane and its analogues in a stable form with broad patent protection over both process and formulation.

While there is substantial clinical evidence that sulforaphane is a highly active compound, it is not currently licensed for pharmaceutical use in any treatment and there are no associated commercial sales.

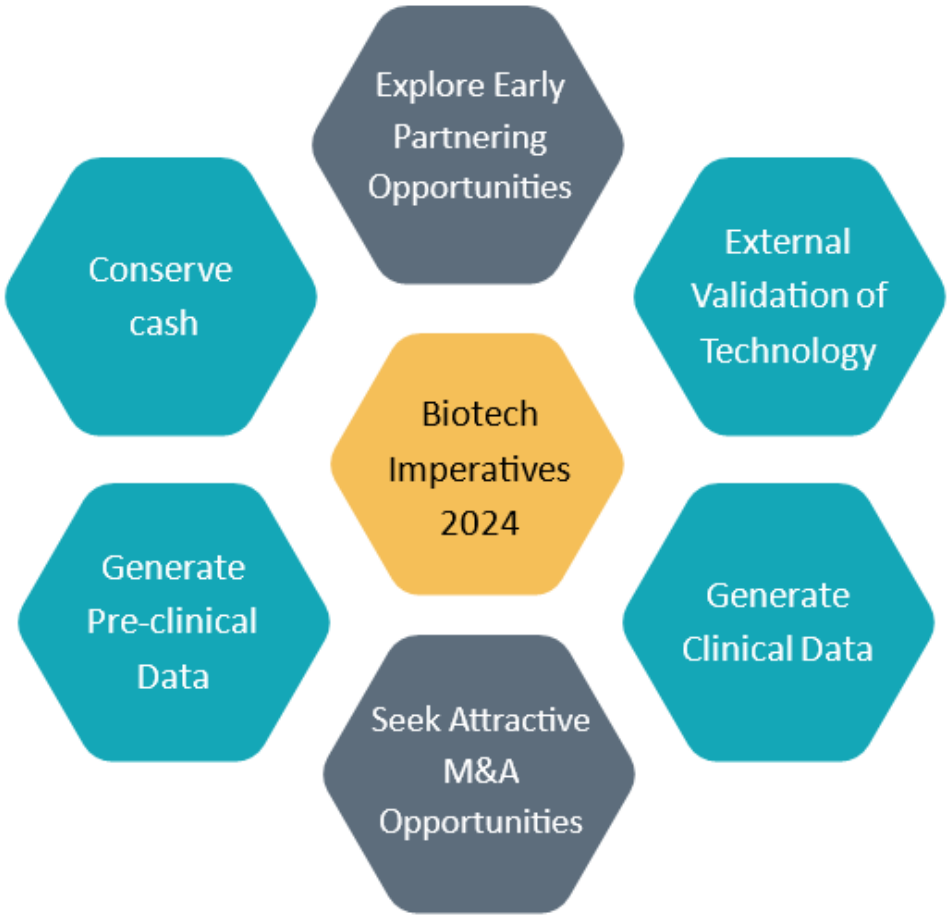
The orexin programme is targeting anxiety and addictive disorders while the DAT programme addresses fatigue, long COVID, MS fatigue, and narcolepsy. Both programme assets also enjoy long dated patent protection.

TheraCryf's main focus is to progress the use of sulforaphane as a clinical therapy in the most effective way while seeking non-dilutive funding to progress the other programmes with a priority to the orexin programme which could enter clinical trials in 2026.

Given the range of possible therapeutic uses, including the growing evidence that sulforaphane works synergistically with radiotherapy in the treatment of cancer, the potential overall market for sulforaphane is huge. For example, sales of Palbociclib, the leading CDK4/6 inhibitor used in the treatment of metastatic breast cancer has sales of over US$5bn pa (see Synthetic sulforaphane). The market potential is also reflected in the overall value of the licensing agreement with Stalicla for the use of sulforaphane in neurodevelopmental disorders. That agreement includes milestone payments totalling up to US$26.5m to the point of initial commercial launch and total milestone payments of up to US$160.5m together with a low-to medium double digit royalty on commercial sales (see Partnerships and collaborations).

Given the known action of sulforaphane, TheraCryf has identified as its focus the treatment of cancer, neurodevelopmental disorders and inflammatory diseases. However, there is significant broader interest in the potential therapeutic benefit of sulforaphane and TheraCryf is open to opportunistic partnerships in other areas where there is a convincing scientific and commercial rationale (Figure 7).

Figure 7: TheraCryf business model



Source: TheraCryf, CAG Research.

TheraCryf's primary strategy is to work with the best investigators involved in relevant pre-clinical work and early-stage clinical trials to develop drugs up to Phase II proof of concept clinical trials. TheraCryf then seeks to out-license to a larger drug company able to support evaluation through the subsequent and significantly more expensive phases of testing ahead of commercialisation. These investigators generally will have their own third-party funding. This approach effectively enables much larger resources to be brought to bear on evaluating the therapeutic use of sulforaphane than TheraCryf could fund on its own. As the Stalicla deal shows, TheraCryf is also willing to enter out-licensing agreements with larger groups at an earlier stage, where that opportunity is available on appropriate terms. TheraCryf also undertakes research and development on its own behalf with a view to identifying the most prospective potential uses of sulforaphane in order to attract relevant investigators and to develop forms of sulforaphane that are more attractive for investigators, such as its new enteric tablet form for which TheraCryf recently funded the successful Phase 1/1b SFX-01 healthy volunteer study.

Synthetic sulforaphane

Natural sulforaphane is highly unstable but TheraCryf's Sulforadex® technology enables the production of clinical grade sulforaphane (SFX-01) in tablet form. Sulforaphane has demonstrated action on three disease pathways. Following the appointment of Huw Jones as CEO, TheraCryf has focused on the use of SFX-01 in the treatment of cancers and neurodevelopmental disease. The company's current drug development pipeline for SFX-01 encompasses breast cancer, Autism Spectrum Disorder, Glioblastoma, Rhabdomyosarcoma and colorectal cancer. More recent trial results indicate that sulforaphane works synergistically with radiotherapy.

TheraCryf has a patented core technology, Sulforadex®, which uses a two-step process starting with a small molecule chemical intermediate called erucin synthesised into pure sulforaphane bound in alpha-cyclodextrin which also forms a ring encapsulating the sulforaphane molecule in a stable framework (Figure 1) suitable for manufacture in tablet form. Alpha-cyclodextrin is glucose based, non-absorbable and widely used for drug formulations.

The Sulforadex® technology is proven, replicable and scalable. Test quantities of SFX-01, TheraCryf's lead asset, are manufactured by a global contract development and manufacturing organisation (CDMO).

Sulforaphane is produced naturally when cruciferous vegetables such as broccoli are chewed when being eaten. The glucoraphanin contained in such vegetables reacts with a human enzyme, myrosinase, to produce sulforaphane. Naturally produced sulforaphane is highly unstable and most research into its effects has been based on natural sulforaphane meaning the dosing regimen has been problematic. Nevertheless, sulforaphane is widely credited with having health giving properties, as referenced for example by The National Library of Medicine, the American Cancer Association and the MD Anderson Cancer Center among others.

Sulforaphane is the subject of numerous pre-clinical and tens of clinical trials including in TheraCryf's own Phase 1b healthy volunteer study using its new enteric coated tablet formation of SFX-01, where it has proven to be very well tolerated in patients at pharmacologically effective concentrations.

Sulforaphane has demonstrated action on three distinct disease-relevant cellular pathways. It is an inhibitor of pSTAT3, which is important in controlling the metastasis of cancer. It promotes the production of Nrf2, a therapeutic target associated with a broad range of diseases which are characterised by excessive oxidative stress and inflammation. Additionally, sulforaphane inhibits SHP2 which is a target relevant in a number of solid tumours and haematological cancers.

SFX-01 is the only pure form of sulforaphane that can be administered as a pharmaceutical and is not to be confused with any niche dietary supplement based on botanical extracts.

Following the appointment of Huw Jones as CEO in 2020, TheraCryf has narrowed its focus to the application of SFX-01 in cancers and neurodevelopmental diseases where there is strong clinical need and attractive commercial opportunity.

Breast cancer

The most advanced programme of research into the efficacy of SFX-01 as a therapy is in breast cancer and particularly into the HR+ and HER2 subtypes which account for around two thirds of breast cancers. Clinical research on patients in a Phase IIa trial conducted between 2016-2019 showed that SFX-01 demonstrated anti-tumour activity in tumours that have progressed on hormone therapy as that had become increasingly ineffective.

Pre-clinical trials of SFX-01 shows anti-tumour activity in models where cancer has developed resistance to CDK4/6 inhibitors which are enzymes intended to interrupt the growth of cancer cells and which are used in combination with hormone therapy. Since the completion of the P11a trial of SFX-01 in metastatic breast cancer, CDK4/6 inhibitors are becoming standard of care in first line metastatic breast cancer treatment. However patients invariably become resistant to such treatment. So, TheraCryf is working with academic collaborators to advance pre-clinical studies on the potential for SFX-01 to extend the effectiveness of CDK4/6 with a view to attracting funding for clinical trials in humans.

Neurodevelopmental disorders

In 2022, TheraCryf signed an out-licensing agreement with Stalicla for the global rights to use SFX-01 in neurodevelopmental disorders and schizophrenia. Neurodevelopmental disorders are currently generally diagnosed based on behavioural assessment without relation to any specific biological criteria and are highly heterogeneous. Stalicla has developed a unique platform (the DEPI platform) which leverages biomedical and clinical data in order to identify biologically distinct populations with a view to matching the appropriate treatment to the appropriate patient. The DEPI platform harnesses patients' biological signatures along with complex data analysis to identify tailored treatment options.

Stalicla is working on the design of a Phase II trial to test the efficacy of SFX-01 on Autism Spectrum Disorder (ASD) where there is clinical evidence that SFX-01 can have a positive impact. The precision medicine approach enabled by the DEPI platform should facilitate the identification of patients who would be particularly responsive to SFX-01, thereby increasing the chances of success in clinical trials and eventual use authorisation. Stalicla recently raised US$17.4m in support of its research programmes.

Glioblastoma

Glioblastoma is the most common type of brain tumour accounting for around a third of all brain cancers and affecting around 5 per 100,000 people. Glioblastoma is highly aggressive with an average time to death after diagnosis of just 14 months and a five-year survival rate of only 5%.

In vitro studies with SFX-01 on human cells showed dose-dependent reduction in proliferation and migration while animal testing saw increased disease-free survival and lengthened tumour progression times, synergistic with radiotherapy.

SFX-01 has been chosen for an Investigator Sponsored Study being led by Dr Marjolein Geurts, neuro-oncologist at the Erasmus University Medical Centre in the Netherlands which commenced in October 2023 following the receipt of substantial grant funding.

If the pre-clinical and investigator sponsored clinical study are successful, TheraCryf expects the trial programme to be continued as a TheraCryf-sponsored trial.

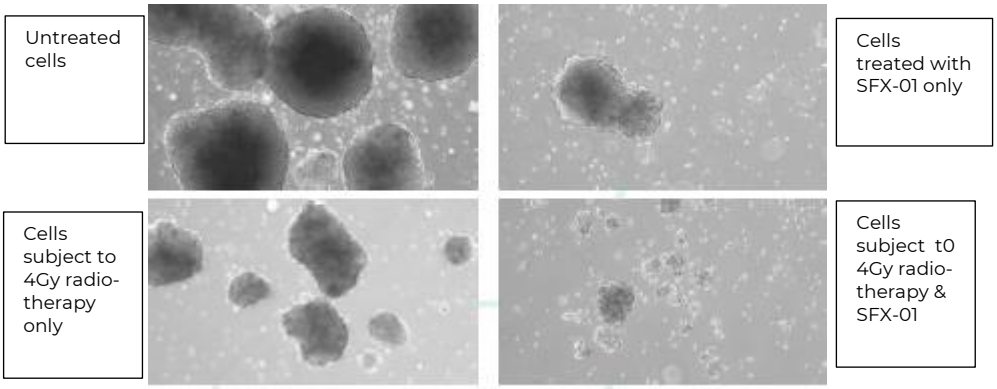
Rhabdomyosarcoma

Rhabdomyosarcoma is a type of soft tissue sarcoma typically affecting children under 10 years old and more common in boys than in girls.

Based on the *in vitro* test results from the work on Glioblastoma which point to the potential of sulforaphane to amplify the effectiveness of radiotherapy, Professor Francesco Marampon of Università La Sapienza di Roma selected SFX-01 for further testing in relation to its potential to improve the outcomes of patients suffering from Rhabdomyosarcoma.

Professor Marampon's work demonstrated that SFX-01 by itself reduced tumour cell growth by inducing G2 cell cycle arrest, so triggering the death of cancer cells (the top right hand panel of Figure 8) as compared to the untreated, radiotherapy resistant cancer (the top left hand panel). While in conjunction with low-dose (4 Gray) radiotherapy treatment, SFX-01 obliterated cancer (the lower right hand panel compared to the lower left hand panel).

Figure 8: SFX-01 impact on radioresistant rhabdospheres



Source: TheraCryf, CAG Research.

Orexin programme

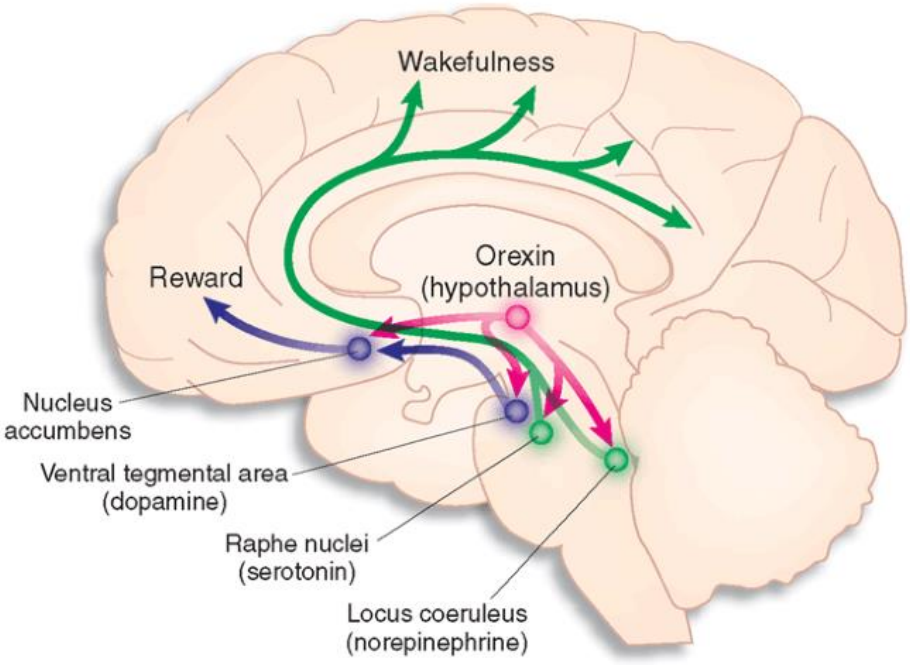
The orexin programme targets addictive disorders. The lead pre-clinical candidate in the programme is an orexin 1 receptor antagonist which is initially targeted at the treatment of Binge Eating Disorder, a condition more common than anorexia and bulimia combined. Prior to its acquisition, Chronos had demonstrated positive pre-clinical proof of concept for the compound via an *in-vivo* model which has a potential annual market value in excess of US$1bn pa. TheraCryf is now seeking non-dilutive funding, most likely by way of grant funding to advance the programme from the pre-clinical to the clinical stage.

The lead clinical candidate in the acquired portfolio is an orexin 1 receptor antagonist whose target is addictive disorders. Prior research by Chronos indicates a potential annual market value in excess of US$1bn pa.

There are two types of orexin receptors, Ox1 and Ox2, found in the central nervous system which play a key regulatory role in many physiological processes, particularly relating to reward and sleep/wakefulness. The action of the orexin system is strongly associated with addictive behaviour. While the action of the receptors is overlapping, the Ox1 receptor is especially associated with reward, feeding behaviour, and anxiety while the Ox2 receptor is associated with sleep/wakefulness.

The receptors are triggered by Orexin-A and Orexin-B which are neuropeptides produced by neurons in the hypothalamus (Figure 9). The Ox1 receptor binds differentially to Orexin-A.

Figure 9: Orexin pathways



Source: Nature Medicine, CAG Research.

Orexin antagonists block the action of the orexin receptors in binding to the Orexin-A and Orexin-B signals generated in the hypothalamus and are a fairly recent development in drug therapy. To date, the principal target condition has been insomnia with Suvorexant, approved for use in the US in 2014, proving successful as it has favourable tolerability and fewer side-effects than

the pre-existing standard of care treatments which had different targets. However, the principal medical need targeted by TheraCryf's orexin programme is addictive disorder.

Suvorexant acts to block both orexin receptors and so is known as a dual orexin receptor antagonist. The primary target of TheraCryf's orexin programme is the Ox1 receptor as the clinical need it is addressing is addictive disorder.

For the compound to be successful it needs to produce a sustained reduction in addictive desire while also avoiding any disproportionate impact on sleep/wakefulness. To do this it needs to be highly selective for the Ox1 receptor over the Ox2 receptor. The initial target condition is Binge Eating Disorder (BED) which is a recognised psychiatric condition. Chronos demonstrated positive pre-clinical proof of concepts for the compound in an *in vivo* model rodent model of binge.

BED is more common than anorexia and bulimia combined and is not treatable with approved anti-obesity drugs. BED involves regularly eating uncontrollably and excessively over a short period of time until the sufferer is uncomfortably full but does not include subsequently purging the food through vomiting, which is the additional characteristic of Bulimia. Binges are sometimes planned in advance but can be spontaneous. The binging is usually done alone and is often associated with guilt or shame, once over.

The only approved drug for the treatment of BED is Vyvanse (Lisdexamfetamine Dimesulate) and it is only approved for use in the US. However, as Vyvanse is amphetamine based it is a class II controlled drug which carries a serious risk of addiction which is particularly pertinent given that some 25% of those suffering from BED have a history of substance abuse.

BED is estimated to affect 1.4% of the population amounting to over 13m people across the US, EU and Japan alone.

Market research by Chronos indicated a peak sales projection for its orexin 1 receptor antagonist of over US$1bn pa in the treatment of BED but it is also anticipated to have potential wider applicability in the treatment of addictive disorders, anxiety, impulse control disorders and post-traumatic stress disorder (PTSD).

TheraCryf is now seeking non-dilutive funding, most likely by way of grant funding to advance its orexin programme from the pre-clinical to the clinical stage.

DAT programme

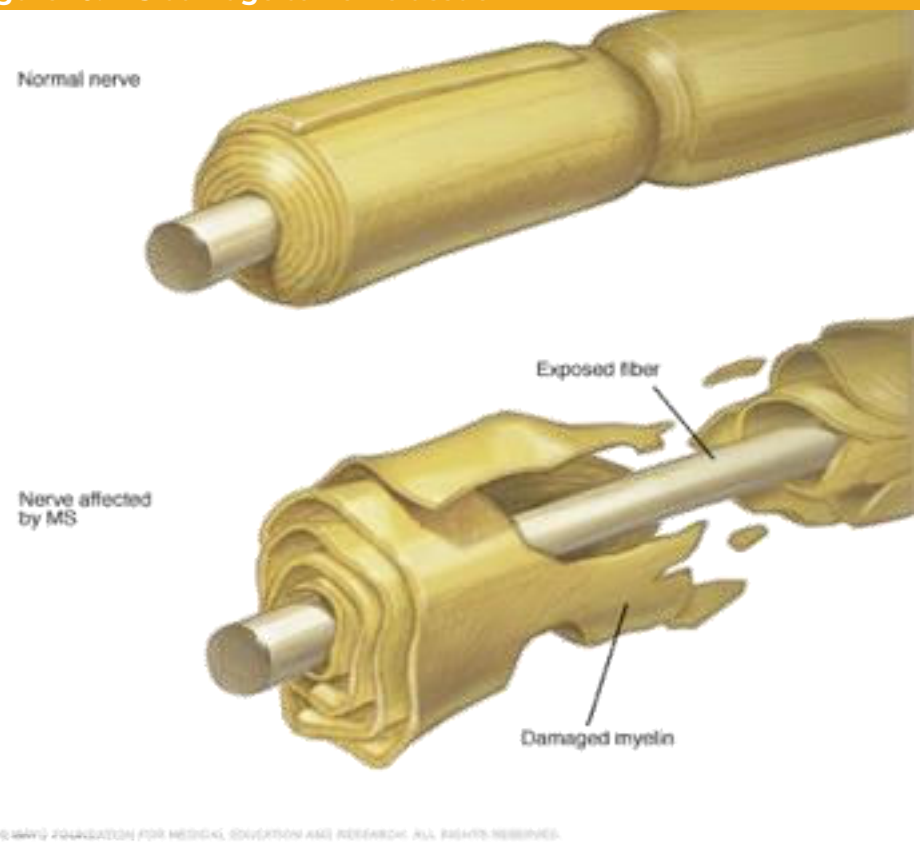
TheraCryf's dopamine transporter (DAT) inhibitor programme is targeting the fatigue commonly associated with multiple sclerosis. The company's DAT inhibitor has been demonstrated and shown to be efficacious in treating animal models of fatigue dosed with the compound. Subject to approval, the potential market in the US alone is estimated at US$400m in a low to medium case. Advancement of the development programme is not expected before 2025, given the focus on the Orexin programme.

The secondary lead asset in the Chronos portfolio, is a selective DAT inhibitor for fatigue associated with multiple sclerosis (MS).

Dopamine (DA) is a key chemical messenger in the brain involved in multiple physiological functions including motor control, emotional state, reward mechanisms, reinforcement of behaviour and some higher cognitive functions. It is often known as the 'feel-good' hormone. Imbalances in dopamine levels are associated with mental health, addiction, Parkinson's disease and obesity.

MS is a chronic disease in which the body's immune system attacks the protective covering on the nerve cells in the brain and spinal cord (Figure 10) with a wide range of symptoms one of which is fatigue. Up to 80% of MS patients suffer moderate to severe fatigue with 50% requiring drug treatment on an unapproved, off-label basis. However, there is currently no drug treatment approved to treat fatigue in MS patients.

Figure 10: MS damage to nerve tissue



Source: Apex, CAG Research.

A dopamine transporter (DAT) inhibitor is a protein that modulates the normal reuptake of the dopamine chemical signal by the neuron which

generated it meaning that dopamine levels are higher than they otherwise would be. Low levels of dopamine in the brain have been associated with feelings of fatigue so the selective blocking of the reuptake of dopamine into the brain by the transporter is intended to cause a gradual increase in dopamine levels in the brain, thus reducing fatigue. This status has been demonstrated and shown to be efficacious in treating animal models of fatigue dosed with TheraCryf's DAT inhibitor.

Were the DAT inhibitor to be approved for use in the treatment of MS, Apex, a healthcare consulting company, estimates potential peak sales in the US alone at US$400m in a low to medium case.

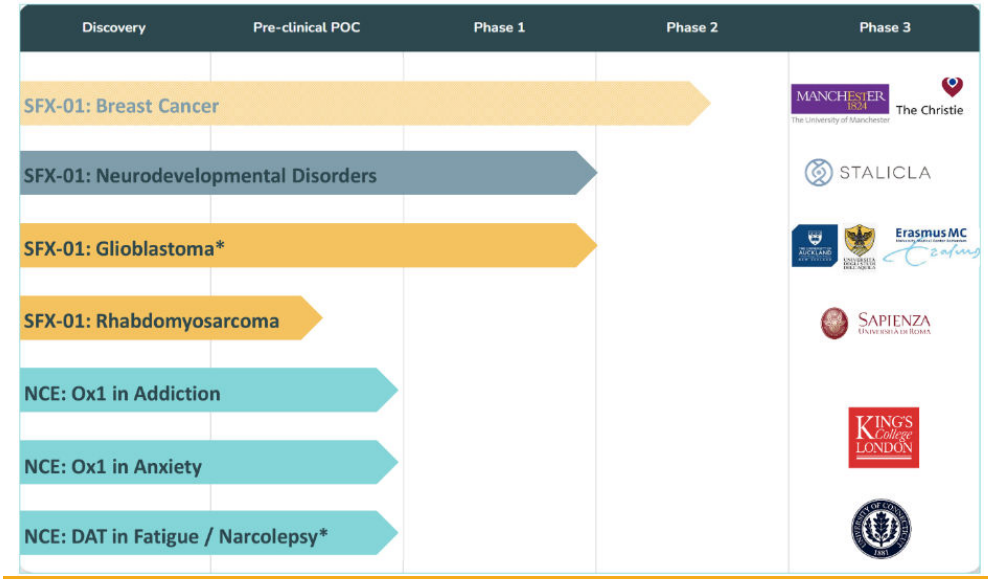
With TheraCryf focusing on advancing the orexin programme, the company does not anticipate resourcing the development of the DAT programme before 2025.

Partnerships and collaborations

In keeping with its strategy and demonstrating the interest in SFX-01 as a therapeutic agent, TheraCryf has eight active academic collaborations together with its Stalicla out-license partnership. TheraCryf is working with Stalicla to commence a Phase 2 trial in Autism Spectrum Disorder. Currently, the most active academic collaborations are with Erasmus University (Glioblastoma), Università La Sapienza (Rhabdomyosarcoma), and the University of Manchester (breast cancer). In addition, the University of Michigan is studying the potential for SFX-01 to prevent colorectal cancer.

Successful partnerships and collaborations are core to TheraCryf's business model (Figure 11) as they are crucial to extending the range of testing, both pre-clinical and clinical, to which SFX-01 can be trialled with a view to establishing successful use cases and future commerciality. Moreover, they are critical in leveraging TheraCryf's own financial ability to fund testing as they bring in third-party funding directly and can help draw in other potential partners, as the spread from the radiosensitisation work on Glioblastoma to Rhabdomyosarcoma demonstrates.

Figure 11: Pipeline and partners



Source: TheraCryf, CAG Research.

The roll of partners and collaborators is distinguished, long and varied. TheraCryf lists nine of them (Figure 11). Of TheraCryf's relationships, currently the most active are those with Stalicla, Erasmus University, Università La Sapienza di Roma, and the University of Manchester. Ongoing work with these partners is likely to provide multiple points of newsflow in 2024/25 (Figure 12), each of which could have a significant impact on the share price together with any new partnerships the company may enter. When TheraCryf initially announced the Stalicla deal, its share price more than doubled.

Figure 12: Potential newsflow 2024/25

Partner/collaborator	Indication/Area	Newsflow
Erasmus U.	Glioblastoma	Results of pre-clinical work
Stalicla	ASD[1]	Launch of P2 clinical trial
Stalicla	ASD[1]	FDA grant of IND[2] status
U. Sapienza	Rhabdomyosarcoma	Radiosensitisation data
U. Michigan	Colorectal cancer	Initial *in-vivo* results
TheraCryf	SFX-01 healthy volunteer study	P1b scientific publication
Kings College London[3]	Orexin programme	Grant funding

Source: TheraCryf, CAG Research. 1) Autism Spectrum Disorder; 2) Investigational New Drug; 3) Potential/other suitable partner.

Erasmus University, Rotterdam

Following the award of grant funding from the KWF Dutch Cancer Society towards a project value of over EUR1m, Dr Marjolein Geurts, neuro-oncologist at Erasmus, has commenced initial pre-clinical trials of SFX-01 in Glioblastoma models to be followed by a clinical Investigator Sponsored Study in Glioblastoma patients. The objective of the study is to establish the presence of SFX-01 in human brain tumours and its engagement with relevant molecular targets in excised tumour tissue. Results of the pre-clinical work are expected to be shared during 2024 with planning for the clinical study during 2025.

Stalicla

The partnership with Stalicla was entered into in 2022 when TheraCryf licensed the global rights for SFX-01 in neurodevelopmental disorders and schizophrenia to Stalicla which is uniquely positioned to be able to identify those patients most likely to respond to treatment.

TheraCryf received US$0.5m on entering the collaboration and is due milestone payments up to commercial launch of US$26.5m with total milestone payments of up to US$160.5m due in relation to the first neurological disorder indication under license. Royalties in the low to medium double digit range would also be payable, including on-licensing by Stalicla.

Payments to date total US$0.5m An additional US$0.5m payment is due on completion of the TheraCryf sponsored human volunteer Phase 1/1b study but this has yet to be received and is under dispute. Further milestone payments are due on the commencement of a Stalicla-funded Phase 2 clinical study in Autism Spectrum Disorder with a potential payment of US$5m due if and when the FDA grants SFX-01 Investigational New Drug status for Autism Spectrum Disorder.

Università La Sapienza di Roma

Following the promising results from the *in vitro* studies on Glioblastoma in which SFX-01 demonstrated a synergistic relationship with radiotherapy, TheraCryf commenced a collaboration with Professor Francesco Marampon of Università La Sapienza di Roma in May 2022. That has since demonstrated SFX-01 to be effective as a single agent on Rhabdomyosarcoma and to amplify the impact of radiotherapy in treating this childhood cancer during *in vitro* testing.

University of Manchester

TheraCryf has a longstanding collaboration with Professor Rob Clarke at the Manchester Breast Centre at the University of Manchester's School of Medical Sciences investigating the potential use of SFX-01 in patients with metastatic breast cancer. Over time, treatment of such cancer with CDK4/6 inhibitors has become the standard of care but resistance to treatment invariably occurs. There is an increasing body of data suggesting that SFX-01 may suppress tumour growth and metastasis in patients who have developed resistance to CDK4/6 inhibitors. The collaboration currently has a number of pre-clinical experiments ongoing, particularly in relation to the inhibition of phosphorylation of the STAT3 protein, believed to have an important role in a number of cancers as activated STAT3 is associated with the proliferation and survival of tumour cells. It is hoped the results will support clinical trial design and/or licensing in patients with HER-2 negative, ER+ve breast cancer where CDK4/6 inhibitors are showing weakening effectiveness.

University of Michigan

TheraCryf started a collaboration in 2022 with Dr Grace Chen of the University of Michigan to investigate the potential anti-tumour effects of SFX-01 in colorectal cancer. Colorectal cancer is considered to be the third most common form of cancer worldwide, with between 1.5-2.0 million annual diagnoses, and is the second leading cause of cancer-related deaths. The collaboration is seeking to evaluate the *in vivo* effects of SFX-01 in models of colorectal cancer. The activity and mechanism of action of SFX-01 on organoid growth, morphology, stemness and inflammatory markers will also be investigated. Initial results of this research are expected to be published this year.

Financials

As a pre-clinical stage drug development company, TheraCryf's revenue is intermittent. Costs peaked in FY23 which included the TheraCryf funded Phase 1b study of the enteric coated SFX-01 tablet formulation and are set to fall c30% in FY24. We expect tight cost control to result in a further c50% YoY reduction in costs prospectively as the company focuses on extending its cash runway through towards the end of FY26. We do not forecast the receipt of any further milestone payments, nor the receipt of any non-dilutive funding which may be generated by the company for the further direct development of its clinical pipeline.

As TheraCryf is a pre-clinical stage drug development company with no established commercial sales, its revenue is intermittent, currently reflecting just the Stalicla milestone payments.

Operating costs excluding expensed R&D but including share based payments totalled £2.2m in FY23 with FY24 likely to be similar before falling to £1.2m prospectively, we forecast. R&D expense of £3.3m in FY23 should fall to £1.8m in FY24 and to £0.8m thereafter. That profile reflects TheraCryf's intention to extend its cash runway through towards the end of FY26 delivered as a result of tight cost control and its ability to pace R&D expenditure in support of its existing collaborations and in evaluating the most prospective opportunities to mature new collaborations, together with the recent equity raise.

In April, TheraCryf completed a net equity raise of around £0.8m in conjunction with the acquisition of Chronos. The initial consideration for Chronos was £0.9m which was satisfied by the issuance of 62.3m consideration shares with a nominal value of 1.44p/share. Further payments of up to £2.5m are due on the achievement of certain milestones payable in stock or loan notes at TheraCryf's election, none of which are expected to be triggered in the near term.

At the time of the fund raise, TheraCryf disclosed cash and net cash of £2m which has now been increased to approximately £3m, we calculate.

The company's R&D effort generates a steady stream of cash tax receipts which have averaged c£0.5m pa over the last five years and which typically cover around 14% of the cost base. However, tax receipts for FY24 will be around twice that level, reflecting the high level of eligible spend in 2023, mainly on the Phase 1b healthy volunteer study with receipts of £0.9m reported with the interim results. While the prospective reduction in R&D spend will also reduce the level of ongoing cash tax receipts, we expect coverage of the cost base to increase to c20%, reflecting the proportionately larger reduction in the cost base.

On our estimates, TheraCryf will extend its cash runway through towards the end of FY26 excluding any additional milestone payments which may become due or any non-dilutive funding which may be generated by the company for the further development of its clinical pipeline (Figure 13 and see Summary financial statements).

Figure 13: Key financials (£k)

Item (March YE)	FY22A	FY23A	FY24E	FY25E	FY26E
Revenue	0	442	400	0	0
Operating expenses	(3,193)	(5,546)	(4,026)	(2,026)	(2,026)
Tax repayment	533	475	913	462	344
Tax repayment as % of opex	17%	9%	23%	23%	17%
Net loss	(2,730)	(4,043)	(3,089)	(1,682)	(1,682)
Diluted EPS	(0.99p)	(1.47p)	(1.12p)	(0.39p)	(0.39p)
Net (cash)/debt	(9,030)	(5,000)	(2,022)	(1,384)	138

Source: TheraCryf, CAG Research.

Valuation considerations

While drug development is inherently a high risk process, were TheraCryf's clinical assets to be approved for medical use, their total market potential is in the multiple-billions of dollars. Nevertheless, by comparison with peers, the market appears to be disproportionately pessimistic about the risks TheraCryf faces. As against eleven peers, TheraCryf has the lowest market capitalisation of the group at just £3m, yet it is potentially due substantial milestone payments to which it trades on by far the least demanding multiples. Moreover, it is one of only six of the group with active ongoing clinical trials and its lead candidate is targeting large, rather than niche markets with multiple share-price significant points of newsflow due through 2025. Moreover, the expanded portfolio adds option value in what is the very active area of neuroscience.

TheraCryf is seeking to commercialise its lead asset, SFX-01, with a focus on the treatment of cancer, neurodevelopmental disorders and inflammatory diseases. While SFX-01 has not yet been licensed for commercial use, interest in sulforaphane as a clinical therapy is high, enabling TheraCryf to enter into multiple academic collaborations and to partner with Stalicla (see Partnerships and collaborators).

SFX-01 has been the subject of a number of Phase 1 trials, and TheraCryf is working with Stalicla to commence Phase 2 trials for the treatment of autism spectrum disorder.

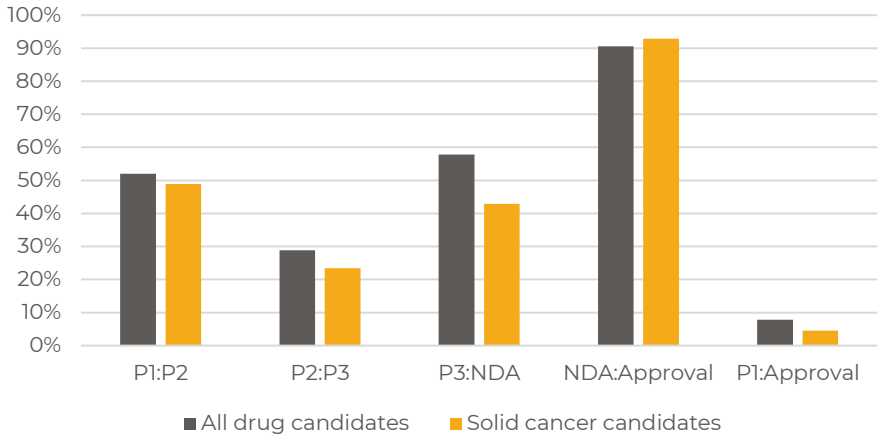
Drug development is inherently a high risk process subject to stringent regulation as all drugs are poisons meaning that they have an impact on body chemistry, otherwise they would be ineffective.

Most drugs fail clinical testing. On average, only one to two of every 10,000 substances synthesised in laboratories will successfully pass all stages of development required to become a marketable medicine (source: efpia).

No drug is ever approved because it is safe. The test is efficacy in relation to other treatments in the context of a risk/benefit approach. During initial pre-clinical and clinical testing, sulforaphane is advantaged compared to novel compounds as it is produced naturally in the body during the consumption of broccoli and other cruciferous vegetables. High tolerability of SFX-01 in humans has been confirmed by TheraCryf's Phase 1b healthy volunteer study. In other studies sulforaphane has demonstrated pharmacological impact on the human body, so the key issue is establishing a specific use case or cases for SFX-01 as an approved therapeutic.

Clinical testing generally proceeds from Phase 1 through Phase 2 through Phase 3 to final approval for a specified use. Figure 14 shows the overall phase transition success rates for all drugs and for cancer drugs targeting solid tumours.

Figure 14: Clinical phase transition probability of success

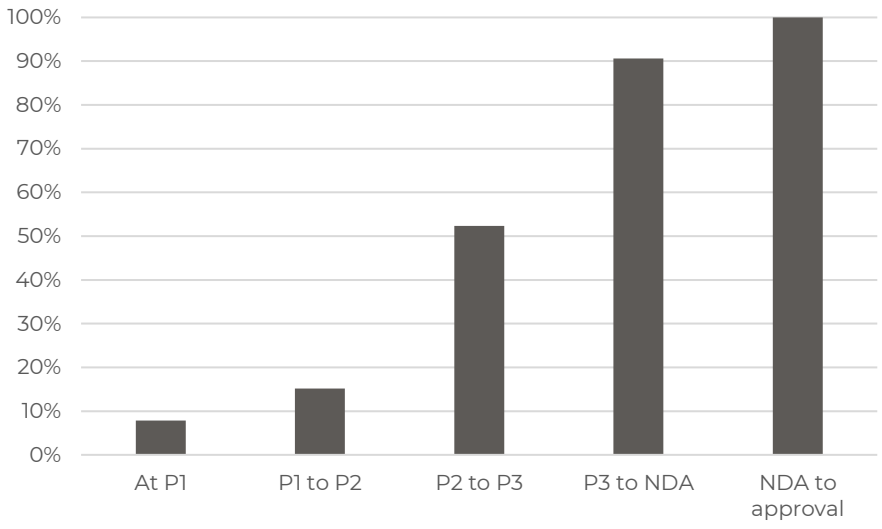


Source: BIO | QLS Advisors | Informa, CAG Research.

The highest level of risk is the transition from Phase 2 to Phase 3 trials. That is because Phase 2 establishes anticipated efficacy, which is the litmus test for regulatory approval, and also marks a critical review point to assess the potential future commercial value ahead of the significant step up in development cost required to undertake Phase 3 trials. Just 28.9% of all drugs and 23.4% of cancer drugs make the transition from Phase 2 to Phase 3 trials meaning the transition from Phase 2 into Phase 3 has the highest rate of failure.

These risks are multiplicative meaning that for a compound in Phase 1, the risk across a therapy making it all the way through to approval is just 7.9% (52.0%*28.9%*57.8%*90.6%=7.9%) based on the risk across all therapies and 4.6% for solid cancer therapies (Figure 15).

Figure 15: Clinical phase transition de-risking (all therapies)



Source: BIO | QLS Advisors | Informa, CAG Research.

Should SFX-01 eventually be approved for clinical use, the total markets it is targeting are scaled in the multiple-billions of dollars.

At TheraCryf's current stage of development we believe it is too speculative to build DCF based models of potential use values to derive a point valuation. However, we can demonstrate that markets appear to be disproportionately pessimistic about the risks TheraCryf faces in achieving significant commercial value compared to other valuations in the market.

Figure 16 lists all companies with a primary listing in the UK, a market capitalisation of under £100m, and whose primary business is drug development.

Figure 16: TheraCryf valuation to peers

Company	Mkt cap (£m)	Disclosed max milestone (US$m)	Disclosed milestone /mkt cap (X)	Disclosed milestone /EV (X)	Sales (£m)	Most advanced current trial	Net cash /(debt) (£m)	Focus
TheraCryf	3.2	161	40.2	312.9	0.4	Phase 1	3.0	Cancer, neurodevelopmental disorder, neuroscience
Scancell	91.6	624	5.4	5.0	5.3	Phase 2	-5.9	Cancer and infectious diseases
Redx Pharma	58.3	755	10.4	14.8	4.2	Phase 2	18.1	Fibrotic disease and cancer
Arecor Therapeutics	41.8	n/d	n/a	n/a	2.4	Phase 1	8.2	Diabetes; reformulating existing therapies using Arestat™ platform
Hemogenyx Pharma	20.6	n/a	n/a	n/a	0.0	Pre-clinical	1.2	Blood disease
Destiny Pharma	16.4	570	27.7	44.7	0.0	Phase 3	6.4	Infection prevention
Synairgen	11.8	n/a	n/a	n/a	0.0	n/a	14.6	Viral lung infection
Bivictrix Theapeutics	9.5	n/a	n/a	n/a	0.0	Pre-clinical	1.9	Cancer
Immupharma	9.2	n/d	n/a	n/a	0.0	Phase 2/3	0.2	Autoimmunity & inflammation; anti-infection
Genflow Bioscience	6.5	n/a	n/a	n/a	0.0	Pre-clinical	0.7	Liver, Werner Syndrome
Roquefort Therapeutics	5.9	n/a	n/a	n/a	0.0	Pre-clinical	0.5	Cancer
ValiRx	4.1	20	3.9	5.0	0.0	n/a	0.9	Cancer, women's health

Source: Companies, CAG Research.

Besides market capitalisation, the table shows the maximum potential milestone payments due under out-licensing agreements, where relevant, together with the relationship between such potential milestone payments to market capitalisation and to enterprise value, whether there is any sales revenue, the clinical stage of the most advanced current trial, the financial position and the focus of the relevant company's drug development pipeline.

Of the dozen companies listed, TheraCryf has the lowest market capitalisation of the group at just £3m and the second lowest EV, yet it is potentially due substantial milestone payments to which it trades on by far the least demanding multiples. Moreover, it is one of only six of the group with active ongoing clinical trials and its lead candidate is targeting large, rather than niche markets.

The other companies with similar characteristics to TheraCryf, as reflected in Figure 16, have market capitalisations ranging from £92m-£16m and dominate the top of the table with the exception of Destiny Pharma.

In our view, Figure 16 demonstrates that TheraCryf, despite having the characteristics common to the most valuable companies in the table, trades

on the lowest market capitalisation and one that is less than many companies with no drug in trial and no drug sufficiently advanced to persuade drug developers to enter into out-licensing agreements. Moreover, given the number of investigations and trials that TheraCryf has in train, there should be multiple points of newsflow in 2024/25 (Figure 12), each of which could have a significant impact on the share price.

The addition of the Chronos portfolio of neuroscience assets trebles the number of clinical assets in TheraCryf's portfolio. Both these programmes also address large potential markets and are in what is currently a very hot area for drug development.

Since the start of 2023 the total value of out-licensing deals, acquisitions and funding transactions in the area of neuroscience exceeds US$23bn and includes some of the largest names in big pharma as well as a host of biotech drug developers (Figure 17).

Figure 17: Neuroscience related transactions

Subject	Target/Funding	Value US$m	Date	Neuroscience target
Pharmanovia	Asxome Therapeutics	167	Feb-23	Sunosi/excessive daytime sleepiness
AstraZeneca	Orexin/AXD4041	n/a	Nov-23	Opiod use disorder, Phase 1 trial
Invidior	C4XD/Orexin	20	Aug-23	Orexin-1 receptor antagonist, C4X_3256
Johnson&Johnson	n/a	n/a	Dec-23	Neuroscience one of four focus areas in Innovative Medicine
AbbVie	Cereval Therapeutics	8.7bn	Dec-23	Various inc schizophrenia, Parkinsons, & mood disorders
Bristol Myers Squibb	Karuna Therapeutics	14.0bn	Dec-23	Schizophrenia
Neurona Therapeutics	Series E financing	120	Feb-24	Epilepsy
Engrail Therapeutics	Series B financing	157	Mar-24	Anxiety disorders, depression, PTSD
Neurosterix	Company launch	63	Apr-24	Allosteric modulators
Seaport Therapeutics	Series A financing	100	Apr-24	Neuropsychiatric medicines/Glyph platform
Reunion Neuroscience	Series A financing	103	May-24	Postpartum depression

Source: Companies, CAG Research.

TheraCryf is now actively seeking non-dilutive funding to advance the drug development pipeline acquired with Chronos with a focus on the orexin programme.

Structure, management, and shareholders

TheraCryf is an AIM listed biotechnology company. Following recent changes, the Board is now comprised of four Directors lead by Huw Jones who became CEO in October 2020. In addition to the Board, TheraCryf is supported by a team of Expert Advisors. The company has a 77% free float. Following the recent fund raise and acquisition of Chronos for stock, there has been considerable change in the share ownership structure, although J Knight remains the largest shareholder with an 8% stake and the balance of disclosable stakes are held by well-known institutional investors in this space.

TheraCryf Pharma plc is a public company incorporated and domiciled in the UK.

TheraCryf listed on the AIM market of the London Stock Exchange (AIM ticker: TCF) in 2015 as Evgen. The company is a member of the AIM all share and health indices and a member of the Numis Alternative Markets total returns index.

TheraCryf is classed as a Biotechnology company under the Industry Classification Benchmark in the Pharmaceuticals and Biotechnology sub-group under Health Care. Within the Bloomberg Industry Classification Standard, TheraCryf is listed as a Speciality Pharma company nested under the Health Care/Biotech & Pharma/Speciality & Generic Pharma/ hierarchy

The Board of TheraCryf applies the Quoted Companies Alliance Corporate Governance Code (the QCA code) for small and mid-size quoted companies to the extent practical, given the group's size and stage of development.

There have been a number of recent changes to Board composition which has been reduced in size from six to the current four Directors including an independent Chair, two Executive Directors and one Independent Non-Executive Director (INED) rather than the minimum of two INEDs recommended by the QCA. Dr Alan Barge was appointed Senior INED following the elevation of Dr Susan Foden to Chair. Those changes have also affected the composition of the Board Committees comprising an Audit and a Remuneration Committee. Given its size, matters concerning nomination are addressed by the full Board, although the need for a separate nomination committee is reviewed regularly.

Further to the acquisition, Chronos has the right to nominate a NED to the Board

The Directors, Board Committees and their current composition are as set out in Figure 18.

Figure 18: Directors, Board Committees, and membership

			Committee/membership	
Member	**Position**	**Date appt**	**Audit**	**Remuneration**
Susan Foden	Chair*	Oct-15	X	X
Huw Jones	CEO	Oct-20		
Toni Hänninen	CFO	Jan 24		
Alan Barge	Senior INED	Oct-15	X	

*Source: TheraCryf, CAG Research. *Non-executive.*

Board and management

Dr Susan Foden – Non-Executive Chair

Dr Susan Foden has a background in science and drug development with a particular focus on oncology. Dr Foden has over 20 years' experience as a NED working with public and private companies including having held NED roles at Vectura plc, and BTG plc. Dr Foden is currently Executive Chair of Australian biotech QBiotics, an Investment Committee member of CD3, the drug discovery initiative between the European Investment Fund and the University of Leuven, and a Trustee of the Roslin Foundation in Edinburgh.

Dr Huw Jones – Chief Executive Officer

Dr Huw Jones has over 30 years' experience of leadership roles in public and private R&D-based companies within the biotechnology and pharmaceutical sector, with a particular focus on pre-clinical and clinical drug development, dilutive and non-dilutive financing, and business development. Dr Jones is a Non-Executive Director of industry body OBN Ltd.

Toni Hänninen – Chief Financial Officer

Toni Hänninen was previously CFO at Faron Pharmaceuticals Ltd, a listed clinical stage biopharmaceutical company. Mr Hänninen has over 20 years of experience in business development and senior finance roles in both public and private companies, working in mature and emerging markets, particularly in Europe and the USA.

Dr Alan Barge – INED

Dr Alan Barge is a Venture Partner at Delin Ventures and is the former chief medical officer of Singapore-based ASLAN Pharmaceuticals PTE. Up until 2011, Dr Barge was vice-president and head of oncology & infection at AstraZeneca and was also chairman of AstraZeneca's Therapy Area Portfolio Team, accountable for the design and delivery of all projects. Prior to his career at AstraZeneca, Alan was European and global medical director for Amgen Inc.

Besides the Executive Directors, TheraCryf's senior management includes Dr Helen Kuhlman who is Chief Business Officer and Dr Glen Clack who is Chief Medical Officer.

Expert Advisors

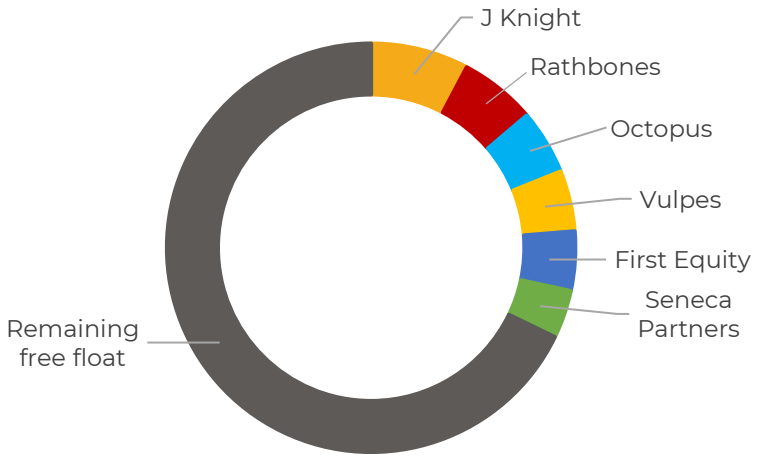
In addition to the Board, TheraCryf is supported by a team of Expert Advisors including, Dr Marjolein Geurts, Dr Claudio Festuccia, Professor Anthony Chalmers and Professor Phil Eaton who while focused on oncology provide TheraCryf with access to a wide range of clinical expertise and contacts. Neuroscience advisors include Professor Alan Young, Dr Fraser Murray, and Dr Timothy Schulz-Utermoehl.

Shareholders

Following the recent equity raise and acquisition of Chronos for stock, TheraCryf has 427m shares in issue and 77% free float. As of the latest AIM rule 26 listing, the largest shareholder is a private individual, J Knight with a

holding of 8%, but the other five holders with positions in excess of 3% are well known institutional investors into companies like TheraCryf (Figure 19).

Figure 19: Shareholders



Source: TheraCryf, CAG Research.

Risks

TheraCryf lists six principal risks which are generic to companies of its type, in our view. We identify development risk as being the most critical. Further clinical development of SFX-01 is largely dependent on third-party investigators while progressing the orexin programme is dependent on additional non-dilutive funding. We do not believe any of the identified risks are currently subject to any significant change, further to the recent equity raise which has extended the cash runway through towards the end of FY26.

TheraCryf lists six principal risks and uncertainties under fairly general headings (Figure 20).

Figure 20: TheraCryf principal risks and uncertainties, CAG view

#	Identified risk	CAG view	Risk direction
1	Development	Generic but critical	No change
2	Commercial & competition	Generic	No change
3	Regulatory	Generic	No change
4	Intellectual Property	Generic	No change
5	Financial	Financed through towards end FY26	No change
6	Operational	Low	No change

Source: TheraCryf, CAG Research.

In our view, most of the risks TheraCryf identifies are generic to companies of TheraCryf's type as a relatively small, drug development company. From an investor perspective, we believe the most important risk is that of failure to be able to realise value from the development of SFX-01. That risk is closely connected to the performance of SFX-01 in trials and the willingness of collaborators and partners to progress their programmes. Within development risk, we note the importance of third-party investigators to the process of advancing SFX-01 towards commerciality.

The acquisition of Chronos trebled TheraCryf's pipeline of drug candidates but progressing the acquired programmes is dependent on the generation of non-dilutive funding.

We do not believe any of these risks are currently subject to any significant change in direction particularly as the recent fund raise has extended the cash runway through towards the end of FY26.

We regard the operational risk as low as TheraCryf has substantial amounts of SFX-01 already manufactured and available which we understand is sufficient to support the multiple research programmes it is currently involved in. Moreover, the Sulforadex® process and established third party supply chain could supply additional volumes as necessary. TheraCryf includes key staff risk within operational risk. The overall team is small and executive management are generally new in their roles having joined with a commitment to commercialise sulforaphane based therapies.

Some companies identify Cybersecurity as an identifiable risk which we believe TheraCryf includes in its operational risk. This is an important risk given the volumes of data produced during clinical trials and the importance of trial data in achieving regulatory acceptance.

Summary financial statements

March year end, £k	FY22A	FY23A	FY24E	FY25E	FY26E
Profit & loss					
Revenue	0	442	400	0	0
Operating expenses	(3,047)	(5,389)	(3,876)	(1,876)	(1,876)
Share based compensation	(146)	(157)	(150)	(150)	(150)
Total operating expenses	**(3,193)**	**(5,546)**	**(4,026)**	**(2,026)**	**(2,026)**
Operating loss	**(3,193)**	**(5,104)**	**(3,626)**	**(2,026)**	**(2,026)**
Finance income	24	98	75	0	0
Pre-tax loss	**(3,169)**	**(5,006)**	**(3,551)**	**(2,026)**	**(2,026)**
Taxation	439	963	462	344	344
Attributable loss	**(2,730)**	**(4,043)**	**(3,089)**	**(1,682)**	**(1,682)**
Basic loss per share	(0.99p)	(1.47p)	(1.12p)	(0.39p)	(0.39p)
Diluted loss per share	(0.99p)	(1.47p)	(1.12p)	(0.39p)	(0.39p)
Cash flow					
Pre-tax loss	(3,169)	(5,006)	(3,551)	(2,026)	(2,026)
Interest (income)/expense	(24)	(98)	(75)	0	0
Depreciation & amortisation	16	13	12	12	12
Share based compensation	146	157	150	150	150
Operating cash flow before working capital	**(3,031)**	**(4,934)**	**(3,464)**	**(1,864)**	**(1,864)**
Delta working capital	**(86)**	**332**	**(500)**	**0**	**0**
Cash used in operations	**(3,117)**	**(4,602)**	**(3,964)**	**(1,864)**	**(1,864)**
Taxation received	533	475	913	462	344
Net cash used in operations	**(2,584)**	**(4,127)**	**(3,051)**	**(1,402)**	**(1,520)**
Monies (to)/from short term investments	1,480	4,520	0	0	0
Interest income	24	98	75	0	0
Acquisition of tangible assets	(3)	(1)	(2)	(2)	(2)
Net cash (used in)/generated from investing	**1,501**	**4,617**	**73**	**(2)**	**(2)**
Net equity issuance	0	0	0	766	0
Net cash generated from financing	**0**	**0**	**0**	**766**	**0**
Implied delta net debt*	**2,563**	**4,030**	**2,978**	**638**	**1,522**
Summary balance sheet					
Total non-current assets	58	46	36	626	616
Net assets	9,227	5,341	2,402	3,036	1,505
Total equity	9,227	5,341	2,402	3,036	1,505
Net debt/(cash) (IAS 17)*	**(9,030)**	**(5,000)**	**(2,022)**	**(1,384)**	**138**
Net debt/(cash) (IFRS 16)*	**(9,030)**	**(5,000)**	**(2,022)**	**(1,384)**	**138**

*Source: TheraCryf, CAG Research. *Fixed term deposits and short term investments treated as cash.*

Capital Access Group
32 Cornhill
London
EC3V 3SG
www.capitalaccessgroup.co.uk