TheraCryf plc

TheraCryf plc (AIM: TCF) is a small-cap biotechnology company developing novel therapies targeting addiction and other neuropsychiatric disorders.

The Company launched on the AIM market in 2015 and in 2024 had a strategic reset after the predominantly share-based acquisition of Chronos Therapeutics. TheraCryf's lead programme, CT-010018, is a selective antagonist of the orexin-1 (Ox-1) receptor, a neural pathway implicated in reward-driven behaviours including binge eating disorder (BED) and substance use disorders, collectively known as addictions. The strategy is to advance CT-010018 through preclinical development and potentially early clinical studies before seeking licensing partnerships with larger biopharma companies, lowering risk while retaining future economic participation in successful programmes. CT-010018 has substance of matter patent protection and has recently applied for manufacturing process patents, which could take exclusivity out to 2046 in major markets, if granted.

In addition to CT-010018, TheraCryf has two further assets. The first is an inhibitor of the brain dopamine transporter (DAT), targeting fatigue associated with neurological and systemic conditions such as multiple sclerosis, long COVID and chemotherapy. The second, SFX-01, is a stabilised formulation of sulforaphane, originally developed when the Company went by the name of Evgen Pharma, which is being explored in autism spectrum disorder (out-licensed) and glioblastoma, including grant-funded research at the Erasmus Medical Centre in Rotterdam.

TheraCryf has recently rejected a non-binding Indicative Proposal to acquire both CT-010018 and the DAT, the Board deciding that it did not reflect the current or future value of the assets. No details on the value of the Indicative Proposal were disclosed, but we feel this provides clear evidence of third-party interest in the underlying assets.

Since 2013, Binge Eating Disorder (BED) has been recognised as a distinct psychiatric diagnosis under the fifth edition of the American Psychiatric Association's (APA) Diagnostic and Statistical Manual of Mental Disorders (DSM-5). The condition affects an estimated 1–3% of adults globally and the global BED therapeutics market has been estimated at approximately USD0.8bn in 2024, growing to around USD1.45bn by 2034, as diagnosis and treatment rates increase (Research & Markets June 2025 Binge Eating Disorder Market Size and Share Outlook - Forecast Trends and Growth Analysis Report (2025-2034). Despite this prevalence, the pharmaceutical market remains relatively underdeveloped, with Vyvanse from Takeda (lisdexamfetamine) being the only drug currently approved for moderate-to-severe BED and only in the USA, although the advent of the GLP-1 analogues for general obesity has significantly raised market awareness, which we believe supports future market development for new effective BED therapeutics.

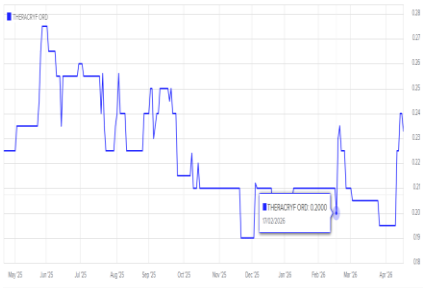
Stock Data
Share Price: 0.24p
Market Cap: £5.16m
Shares in issue: 2.149bn
52 week high/low: 0.30/0.18p

Company Profile
Sector: Health Care
Ticker: TCF.L
Exchange: AIM

Activities
TheraCryf PLC ('TCF', 'TheraCryf', 'the Group') is a biotechnology company focused on developing medicines for addiction and other neuropsychiatric disorders.

Website: www.theracryf.com

12-month share price performance



5-year share price performance

Source: LSE

Past performance is not an indication of future performance.

Turner Pope contact details
Tel: 0203 657 0050
Email: info@turnerpope.com
Web: www.turnerpope.com

Andrew Thacker/Guy McDougall
Corporate Broking & Sales

Stuart Harris
Research Analyst

TPI acts as Joint Broker to TheraCryf plc.

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Investment Thesis:

1. CT-010018 targets the orexin-1 receptor, a regulator of reward and craving pathways in the brain that are implicated in compulsive behaviours including BED and substance addiction. By modulating neural circuits associated with craving and relapse, Ox-1 antagonism or blockade offers a differentiated therapeutic approach compared to treatments focused primarily on appetite suppression or metabolic pathways, such as the GLP-1 analogues, or stimulant-based therapies, such as Vyvanse. The critical feature of an Ox-1 antagonist is minimal antagonism of the other orexin receptor, Ox-2, which is associated with sedation/somnolence. Management believes CT-010018 is the most selective Ox-1 antagonist discovered, suggesting minimal potential for these side effects.

2. CT-010018 is advancing through Investigational New Drug (IND) and Clinical Trial Application (CTA) enabling studies, including manufacturing scale-up (a GMP-compliant production run of 2.57kg of human grade drug substance has just been completed, with the achieved yield being higher than expected and three weeks earlier than anticipated) and regulatory toxicology work. The Company is targeting readiness for regulatory submission for first-in-human studies during 2026, with several development milestones expected over the next 12–18 months. A complete preclinical package ahead of partnering discussions would represent an important value inflection point.

3. TheraCryf operates as a virtual biotechnology company, outsourcing development activities to specialist CRO and manufacturing partners. The strategy is to advance programmes to early clinical proof-of-concept before seeking licensing partnerships with larger pharmaceutical companies, potentially generating upfront payments, development milestones and royalty streams.

4. After a prolonged period of reduced investment, there are signs of renewed pharmaceutical interest in neuroscience, particularly in areas with clearer biological validation and commercial potential. This is evidenced by a number of high-value transactions in 2023 and 2024, including Bristol Myers Squibb's acquisition of Karuna Therapeutics, AbbVie's acquisition of Cerevel Therapeutics and Biogen's acquisition of Reata Pharmaceuticals, alongside a broader increase in CNS-focused partnering activity. While the recovery remains selective rather than broad-based, these developments suggest that differentiated early-stage assets addressing neuropsychiatric disease may once again attract meaningful strategic interest from larger biopharma companies.

5. In addition to the Ox-1 programme, TheraCryf is developing a brain dopamine transporter (DAT) modulator targeting fatigue associated with neurological diseases and conditions such as multiple sclerosis and chemotherapy-induced fatigue. The Company also retains rights to SFX-01 in glioblastoma and other indications, which is currently being advanced, primarily through academic and grant-funded collaborations.

6. With a market capitalisation of approximately £4–5m, the Company trades slightly higher than its end-September 2025 cash balance while progressing its lead programme toward clinical entry. Positive clinical data or the signing of a licensing partnership could materially re-rate the shares from current levels. We conservatively see fair value of the company at around 0.6p per share (market cap of ca. £15m), which is derived from the Ox-1 and DAT programmes, and would expect that to be realised over the next 12 months as the preclinical package for CT-010018 is delivered. This valuation is based upon a DCF of the two main programmes with a conservative 5% probability of success and 15% discount rate, and does not reflect that the average up-front payment in CNS out-licensing deals is around £20m and rises to £38m with phase 1 data delivered.

Risk Warning: Potential valuations and price targets are based on financial modelling and there is no guarantee that such valuations, financial forecasts, or price targets will ever be realised, therefore please do not base your investment decisions on these alone. Also please note that past performance is not a reliable indicator of future results.

7. TheraCryf reported cash of approximately £3.5m as of September 2025, which management expects will fund the development activities required to bring the Ox-1 programme to clinical readiness by the end of 2026.

8. TheraCryf is led by a highly experienced board and management. CEO Dr Huw Jones is a thirty-five-year veteran of the Pharma and Biotech industry, and Dr Alastair Smith, the Board Chair, is an equally experienced biotech CEO with a record of success, notably in Avacta Group plc. The team as a whole has a significant track record of successful drug discovery, development, monetisation and commercialisation of novel medicines.

Executive Summary

Company background and evaluation

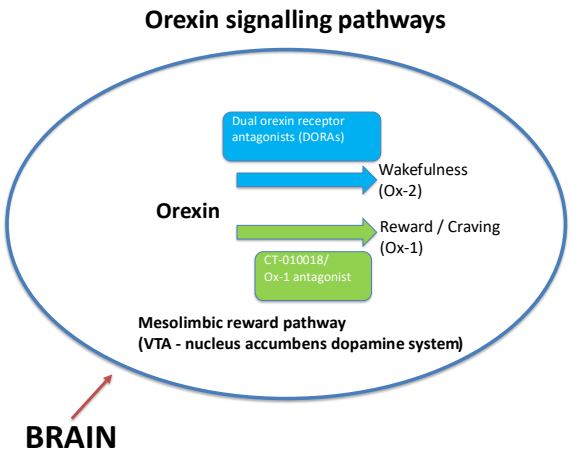
TheraCryf plc is an AIM-listed (October 2015, as Evgen Pharma), early-stage biotechnology company focused on the development of therapeutics for addiction and related behavioural brain disorders. Following its 2024 strategic reset, including the acquisition of Chronos Therapeutics and renaming from Evgen Pharma, the Group has transitioned from its legacy oncology focus to a neuroscience-led pipeline, with CT-010018, an orexin-1 (Ox-1) antagonist, being the core value driver.

TheraCryf's stated strategy is to advance assets through preclinical and early clinical inflection points before securing partnerships with larger biopharma companies, with potential for upfront payments, development milestones and royalty streams.

We see the principal TheraCryf investment case being based on Ox-1 antagonism as a differentiated approach to treating binge eating disorder (BED) and substance addiction. BED is estimated to affect approximately 1–3% of adults globally, yet pharmacological treatment remains relatively underpenetrated, with revenues of around USD800m in 2024 and forecast to grow to c.USD1.45bn by 2034. The overall addiction treatment market was estimated at around USD9.4bn in 2024 and is expected to reach USD16.2bn by 2034 (Precedence Research July 2025 Addiction Treatment Market Size to Hit USD 16.22 Billion by 2034). Current pharmacological options are limited, with Vyvanse (lisdexamfetamine) the only approved therapy for moderate-to-severe BED, and newer GLP-1 therapies primarily targeting appetite and metabolic pathways rather than the underlying compulsive behaviour.

Orexin is a well-characterised neuropeptide system involved in regulating arousal and behaviour, and has already been successfully targeted in sleep disorders through dual orexin receptor antagonists (DORAs), which act primarily via Ox-2 inhibition. Approved drugs include Belsomra (suvorexant) from Merck, Dayvigo (lemborexant) from Eisai and Quviviq (daridorexant) from Idorsia, which collectively generated annual global sales in excess of USD1bn in 2025. Ox-1 is more closely linked to reward-driven behaviour, including craving and relapse, and its inhibition may reduce compulsive behaviour and sensitivity to triggers such as stress or environmental cues, which underpins the company's lead programme.

Figure 1: Orexin signalling pathways



Source: Author illustration

TheraCryf is advancing CT-010018 through Investigational New Drug (IND) and Clinical Trial Application (CTA) enabling studies, with a clear execution plan encompassing Good Manufacturing Practice (GMP) scale-up, regulatory toxicology and first-in-human trial preparation. Preclinical progress has been encouraging, including maximum tolerated dose studies in two species with no adverse findings at doses up to 1 g/kg, alongside successful scale-up from 0.5 kg to multi-kilogram Good Manufacturing Practice (GMP) batches (a GMP-compliant production run of 2.57kg of human grade drug substance has just been completed, with the achieved yield being higher than expected and three weeks earlier than anticipated). Management is targeting readiness for regulatory submission in 2026, with the next 12–18 months expected to deliver a steady flow of de-risking and value-enhancing milestones.

Beyond CT-010018, TheraCryf is also developing:

1. A brain dopamine transporter (DAT) inhibitor targeting fatigue across neurological and other indications, such as multiple sclerosis, narcolepsy and chemotherapy.

2. SFX-01, a stabilised sulforaphane formulation, for glioblastoma (GBM) and neurodevelopmental disorders. SFX-01 is the main legacy Evgen programme and is largely supported through partnerships and includes a licensing agreement with potential milestones of up to USD160.5m in neurodevelopmental indications (from private Swiss company, Stalicla SA). In October 2022 TheraCryf received an initial $0.5m licensing fee from Stalicla for the asset, and in February 2024 lodged a Notice of Dispute for an additional $0.5m, which it believes is owed after the completion of human volunteer Phase 1b studies. We understand that both sides are speaking amicably and we would hope for a resolution in due course.

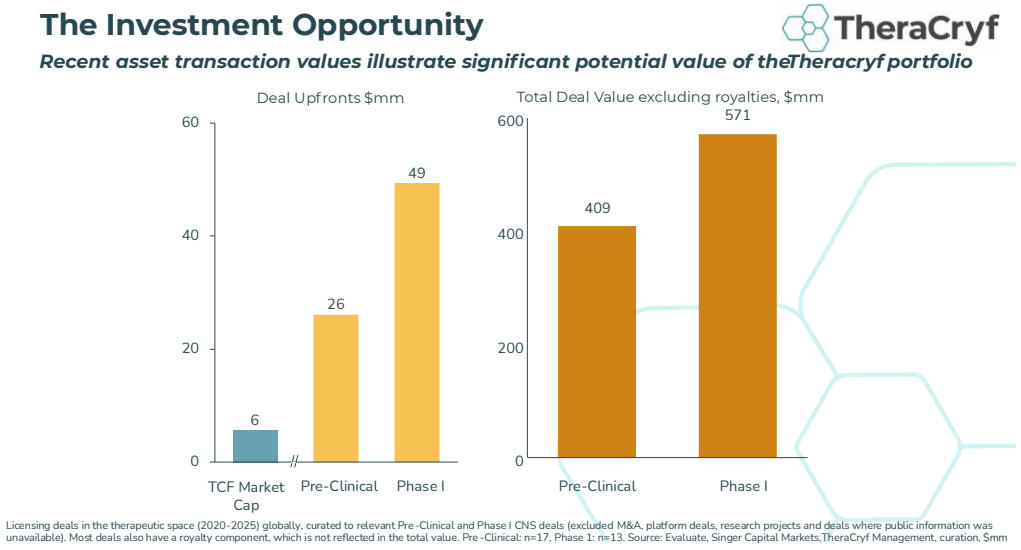
Operationally, the Company follows a capital-efficient “virtual biotech” model, outsourcing development to specialist Contract Research Organisations (CROs) and manufacturing partners. Financially, TheraCryf reported cash of approximately £3.5m as of 30th September 2025 (H1 results for the year to March 31st 2026), with a market capitalisation of c.£4.5m and a reduced operating cost base (FY25 opex c.£2.1m vs c.£4.0m in FY24 and c. £5.5m in FY23), implying runway into late 2026 as CT-010018 approaches clinical trial readiness, despite an expected modest ramp in 2026 as the manufacturing scale up expands with CRO/CDMO Pharmaron.

Valuation

At current levels, the Company trades slightly above its last disclosed cash balance at 30 September 2025, while progressing its lead asset, CT-010018, toward clinical entry. We see a fair enterprise value at around 0.6p per share versus today's 0.2p. This is arrived at using an explicit DCF out to 2040, with conservative forecasts for CT-010018 and the DAT inhibitor (and nothing as of yet for SFX-01), an aggressive risk adjustment (5% chance of success for both) and a 15% discount rate. If the data for CT-010018 comes through in 2026 and it is ready to move to Phase 1 clinical studies, with or without a partner, this would likely move our probability of success from ~5% toward early clinical ranges (~10–15%).

As noted on the front page, our valuation does not fully reflect the average upfront payments for licensed CNS assets, which are typically around £20m for a pre-clinical programme rising to £38m once Phase 1 data are delivered.

Figure 2: Average value of payments of out-licensed CNS assets



Source: Company presentation

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Conclusion

Post the strategic reset in 2024 and pivot from oncology to neurology we feel that the investment case for TheraCryf is much clearer. Small cap biotech oncology development is notoriously difficult, the bar having been set high by large global biopharmas and their multi-billion USD R&D budgets, particularly in a field such as breast cancer post the emergence of precision targeting therapeutics towards specific gene sequences. On the other hand, neuropsychiatry is a more open field, with less companies focussing in a space that is currently dominated by generics. The orexin pathway is well understood and has been developed in the field of sleep, with commercially successful products from Merck, Eisai and Idorsia, but there is limited competition looking at the Ox-1 antagonism for addiction, despite the large market potential.

The Company has a well-structured and funded plan to get CT-010018 ready for clinical studies, with pre-clinical data expected in 2026, at which point TheraCryf will be ready for partner negotiations. Beyond CT-010018 there are the DAT inhibitor for fatigue and SFX-01 for NDDs, both of which have supportive science behind their developments. SFX-01 is still being pursued for GBM, a tumour where there have been few major developments for a number of years and prognosis for patients is still poor. This programme is largely grant funded and therefore represents limited risk and asymmetric upside for TheraCryf and its investor base.

Using conservative forecasts, significant risk adjustments and an aggressive discount factor, we see a fair value of TheraCryf at around 0.6p per share, versus today's 0.2p. Once the preclinical data package is available this year, particularly now the manufacturing scale-up feasibility studies are completed, we see the potential for a significant increase in the share price. Any potential additional funding from a partner who licensed CT-010018 would lead to further development possibilities for the DAT inhibitor. In the background, and assuming it secures adequate funding, Stalicla should continue its work on SFX-01. Phase 1/2 data could potentially be available later in 2026, which, if positive, would raise the probability of the future realisation of USD160m in milestones and license fees. The work on SFX-01 in GBM is largely grant-funded (such as the work being undertaken at the Erasmus Medical Centre in Rotterdam looking at activity in GBM tissue samples), meaning that progress can be made with minimal capital allocation.

CT-010018 for addictive behaviours

TheraCryf's lead programme, CT-010018, is a novel Ox-1 receptor antagonist being developed for addiction and related behavioural brain disorders, initially targeting BED and subsequently alcohol and other addictions. The Company has highlighted preclinical proof-of-concept, including in a BED model, to support this positioning. Over the next 12 months the key news flow is expected to be related to CT-010018 and the continued manufacturing scale-up and completion of IND/CTA-enabling work with the Company's CRO/CDMO contractor for this project, Pharmaron.

Binge eating disorder – an overview

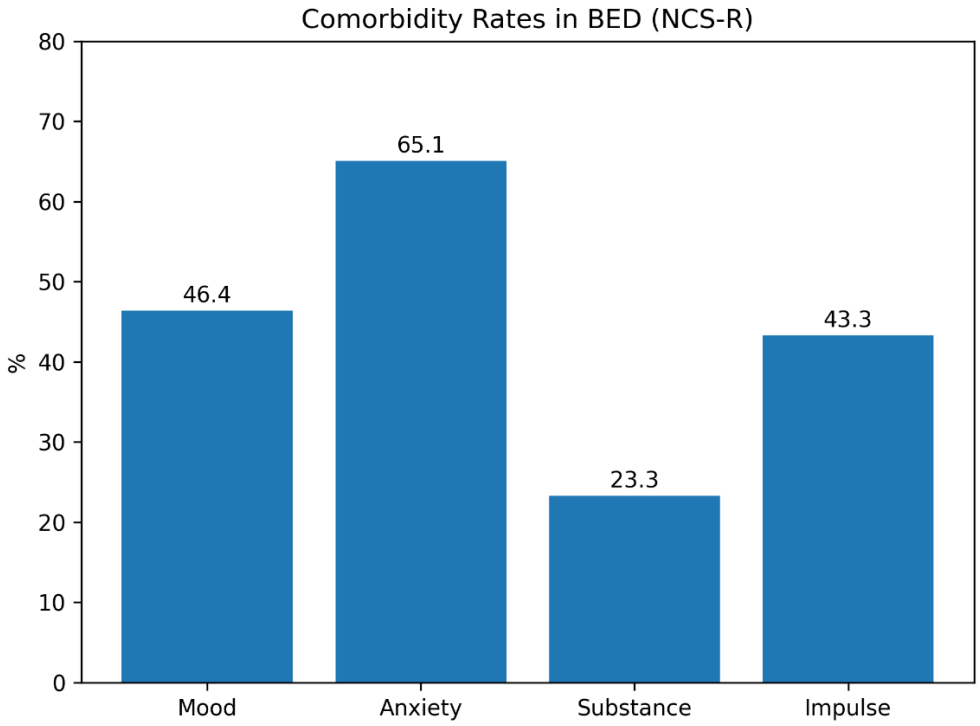
Binge eating disorder (BED) is characterised by recurrent episodes of eating an unusually large amount of food in a short time with a sense of loss of control, followed by marked distress and, unlike bulimia, without regular compensatory behaviours like vomiting, fasting, or excessive exercise. BED is often described as an impulsive-compulsive disorder involving dysregulation in the brain systems that govern reward and motivation and the reaction to environmental cues, so binges can become habit-like and relapse-prone and not related to true hunger. The condition is estimated to affect approximately 1.0–1.5% of women and 0.3–0.8% of men on a one-year prevalence basis, equating to a global patient population of c.30–50 million individuals. Despite this, the current pharmaceutical market remains relatively underpenetrated, with global revenues of approximately USD800m in 2024/25, largely driven by Vyvanse. Forecasts suggesting growth to c.USD1.45bn by 2035 appear conservative in our view, given the combination of increasing diagnosis rates following formal recognition of BED in DSM-5, limited suitability of existing stimulant-based therapies and the broader impact of GLP-1 adoption in increasing awareness and medical engagement with disordered eating behaviours. On a more realistic penetration assumption, we believe the addressable market could expand into the USD2–5bn range over the medium term.

BED treatment

Psychotherapy is the current first-line standard of care in BED, with the gold standard generally considered eating-disorder–focused cognitive behavioural therapy (CBT). The American Psychiatric Association (APA) recommends CBT (or interpersonal therapy, IPT) for patients with BED, reflecting broad evidence that these approaches reduce binge frequency and eating-disorder psychopathology.

However, CBT's shortcomings are practical and clinical. CBT requires trained therapists and repeated sessions, so access and adherence can be limiting; many patients face long waits, cost barriers, or limited specialist availability. Clinically, while CBT is strong at reducing binge episodes, it can be less reliable for weight loss and may not fully address the biology of craving/compulsivity in all patients, particularly when BED coexists with depression/anxiety, ADHD traits, substance use disorders, or significant obesity, where relapse risk can be higher and multimodal care is often needed. The US National Comorbidity Survey Replication found that 78.9% of adults with lifetime BED met criteria for at least one other core disorder (as defined by the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders), broken down by group to be: 65.1% any anxiety disorder, 46.4% any mood disorder, 43.3% any impulse-control disorder and 23.3% any substance use disorder. These incredibly high rates of comorbidity show the importance of holistic care, potentially including pharmacotherapy, when it comes to patients with BED.

Figure 3: Bar chart demonstrating comorbidity rates in BED



Source: Author illustration based on Hudson et al., 2007 (National Comorbidity Survey Replication)

Vyvanse in BED

When pharmacotherapy is used, Vyvanse (lisdexamfetamine) from Takeda was approved in the US in 2015, and is widely cited as the only FDA-approved medication specifically for moderate-to-severe BED in adults. However, its stimulant profile creates real-world limitations: the label carries a prominent "abuse, misuse and addiction" warning and requires ongoing reassessment/monitoring for misuse risk, particularly relevant because, as discussed previously, BED often sits in a broader pathology of impulsivity and comorbidities. Adverse reactions, reported in greater than 5% of patients in studies and at a rate of twice that of placebo, are listed on the US label as dry mouth, insomnia, decreased appetite, increased heart rate, constipation, feeling jittery and anxiety. The USA is the only major market where pharmacotherapy is approved for the condition. Elsewhere Vyvanse (Elvanse in many other international markets, including Europe) has only been approved for ADHD, not for BED, further highlighting the upside potential for an approved pharmacotherapy.

BED is increasingly framed within a larger "addiction-like" theme: recurrent loss of control, powerful cue-driven urges and stress-triggered relapse patterns. This does not imply BED is identical to substance addiction, however it does mean there is overlap in neural circuitry (reward, stress, habit formation) that can be pharmacologically targeted. This is where orexin (hypocretin) biology, and specifically orexin-1 receptors (OX1R), become relevant, as evidenced in multiple reviews and mechanistic papers linking OX1R signalling to drug seeking and cue-induced reward behaviours (e.g. Mahler SV, Moorman DE, Smith RJ, James MH, Aston-Jones G. *Motivational activation: a unifying hypothesis of orexin/hypocretin function*. Nature Neuroscience. 2014;17(10):1298–1303).

If the preclinical and manufacturing data for CT-010018 are supportive and a partner is on-board, clinical development in BED is relatively well-defined, with trials typically using reduction in binge eating days per week as a primary endpoint over 10–12-week treatment periods. Phase 2 studies generally enrol 100–250 patients, followed by two pivotal Phase 3 trials of approximately 300–400 patients each, resulting in a total development timeline of around 3–5 years for a novel agent. As such it is reasonable to believe that, if trials are supportive, a commercial launch could take place in the early 2030s.

GLP-1 usage in BED

The rapid penetration of the GLP-1 analogues Wegovy (semaglutide) and Mounjaro (tirzepatide), is now reshaping the BED market conversation, despite these drugs not being broadly established with BED-specific approvals. Mechanistically, GLP-1s reduce appetite and can influence reward-related feeding; systematic reviews and emerging clinical literature increasingly discuss GLP-1 analogues as potential pharmacotherapies for binge-spectrum symptoms, but the evidence base is still developing, heterogeneous and not yet a clean replacement for BED-validated endpoints and long-term psychiatric outcome data. In parallel, real-world uptake has created a new dynamic, with many patients with binge symptoms being treated in obesity channels. This sometimes occurs without the same depth of eating-disorder screening and psychological support that specialty eating disorder services emphasize, which introduces both opportunity (symptom reduction for some) and risk (worsening or triggering disordered eating patterns in vulnerable individuals).

Commercially, GLP-1s are pulling BED-adjacent demand toward metabolic clinics and weight-management pathways and they raise patient and prescriber expectations for "rapid control" over eating behaviour. That can indirectly pressure BED-focused drug development in two opposing ways: (1) it increases willingness to use medication for compulsive eating (a tailwind for new mechanisms if they can show clear psychiatric benefit and durability); but (2) it creates a higher bar for differentiation, where new BED drugs must justify value not only against CBT/Vyvanse, but also against the perceived broad benefits of GLP-1s on weight, cardiometabolic risk and appetite.

The resulting gap many stakeholders now talk about is "reward/craving/cue reactivity": GLP-1s may reduce appetite and food noise for some, but they may not reliably address relapse-prone, stress- and cue-driven compulsive intake in all patients, especially those whose BED behaves more like an addiction phenotype.
It is worth noting that not all BED patients are obese and in this case the loss of lean muscle mass often associated with GLP-1s makes the approach sub-optimal.

Stimulants vs Ox-1

Vyvanse (lisdexamfetamine) and OX1R antagonists are almost completely opposed in how they approach BED/addiction biology. Vyvanse is a stimulant prodrug converted to dextroamphetamine, which increases release of synaptic neurotransmitters (dopamine/norepinephrine). Amphetamines are crude anorexiants, suppressing all appetite. Clinically, that can reduce binge frequency in some patients, but it does so by broadly increasing arousal/attention-control systems, while carrying predictable trade-offs for a stimulant class, as previously discussed.

By contrast, OX1R antagonists aim to dampen the motivational "pull" of cues and stress that drives compulsive behaviour, rather than boosting monoamine neurotransmitters indiscriminately as seen with amphetamines. In addiction models, OX1R blockade has repeatedly been shown to reduce cue-induced reinstatement (a relapse proxy) and, in some settings, reduce high-motivation drug seeking. The functional profile satisfies BED pathology as an "addiction-adjacent" disorder, with many patients describing binges as cue-triggered episodes of loss of control, where craving, stress and habit-like responses dominate more than homeostatic hunger.

Where OX1R antagonists could have a therapeutic advantage (if human efficacy matches the preclinical signal) is in targeting this relapse vulnerability and compulsive drive, the piece of BED/addiction pathology that psychotherapy and stimulants don't always fully address. The hoped-for differentiation is a medication that reduces binge/craving propensity when it's most problematic (stress/cue periods), potentially without stimulant-like activation and with a lower intrinsic propensity to reinforce "wanting" circuitry. Preclinical work with selective OX1R antagonists has shown reductions in nicotine self-administration and cue-induced reinstatement (repeat of previously extinguished behaviour in response to an environmental trigger), with a similar effect on cocaine use.

OX1R antagonist mechanism of action

OX1R antagonists are small molecules designed to block signalling at the orexin-1 receptor, one of two receptors (OX1R and OX2R) activated by the neuropeptides orexin-A and orexin-B originating in the hypothalamus of the brain, innervating selective parts of the alerting and reward systems in the cerebral cortex. Orexin neurons can act to boost arousal and motivational reward towards the external stimulus. In general terms, OX1R is more commonly linked in the literature to reward-seeking and cue-driven motivation, whereas OX2R has a stronger association with sleep/wake stability and arousal (which is why dual orexin antagonists have succeeded in insomnia).

Mechanistically, blocking OX1R is not primarily about pleasure reduction, rather dampening the craving processes that characterise addiction, particularly cue-induced craving, stress-triggered escalation and relapse-like behaviour. Reviews in the field emphasize that orexin signalling often exerts outsized effects when behaviour is driven by high motivation (e.g. when cues, stress, or effort requirements are high), and comparatively smaller effects on low-effort consumption, for example normal eating patterns in a BED patient. Where this shows up most clearly is in preclinical addiction models. The role of Ox-1 signalling in reward and relapse has been extensively characterised using selective antagonists such as the first generation OX1R-

antagonist SB-334867, originally developed by GlaxoSmithKline (*Smart et al., Br J Pharmacol, 2001*). SB-334867 was a research tool compound that demonstrated proof-of-concept for OX1R antagonism in preclinical models, but was not suitable for clinical development due to suboptimal pharmacokinetics and broader limitations in its drug-like profile, including insufficient brain exposure and developability characteristics. There is other work implicating specific nodes like the ventral tegmental area (VTA) within the human mid-brain and connected dopamine-related motivational signalling (Mahler SV, Moorman DE, Smith RJ, James MH, Aston-Jones G. *Motivational activation: a unifying hypothesis of orexin/hypocretin function*. Nature Neuroscience. 2014;17(10):1298–1303). Collectively, these data support the rationale for development of OX1R antagonists such as CT-010018 in addictive disorder such as BED.

A further nuance emerging in more recent work is that orexin's role in relapse and stress-linked motivation may depend on its interaction with other neuromodulators (dopamine, dynorphin/opioid systems, cannabinoids), and on where/when orexin neurons are recruited. This matters for drug development because it suggests OX1R antagonists might be most effective in defined clinical contexts (e.g., relapse prevention, cue/stress-triggered craving) rather than as universal "anti-use" agents, potentially shaping trial endpoints, patient selection and combination strategies, and increasing the likelihood of a successful clinical trial for the appropriate drug.
In conclusion, we see Ox-1 inhibition as a credible and differentiated therapeutic approach in the treatment of addictive behaviours and the position of CT-010018 as encouraging, for a number of reasons:

1. The global market for pharmacological treatment of addiction disorders is well-established but fragmented across multiple indications, including nicotine dependence, alcohol use disorder and opioid addiction. Forecasts suggest an addiction treatment market of some USD16.2bn by 2034 (Precedence Research July 2025). Despite existing psychotherapeutic and pharmacological interventions, treatment outcomes remain suboptimal in many patients, with limitations in both efficacy and tolerability supporting the need for novel approaches.

2. BED is a recognised psychiatric condition under the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders (DSM), with limited pharmacological treatment options. Lisdexamfetamine (Vyvanse) remains the only approved therapy for moderate-to-severe BED, and only in the USA. The market is estimated at approximately USD800m in 2025 and forecast to reach c.USD1.45bn by 2035. However, given the reported prevalence and increasing clinical focus on obesity and related conditions, we believe the addressable market may be larger over time.

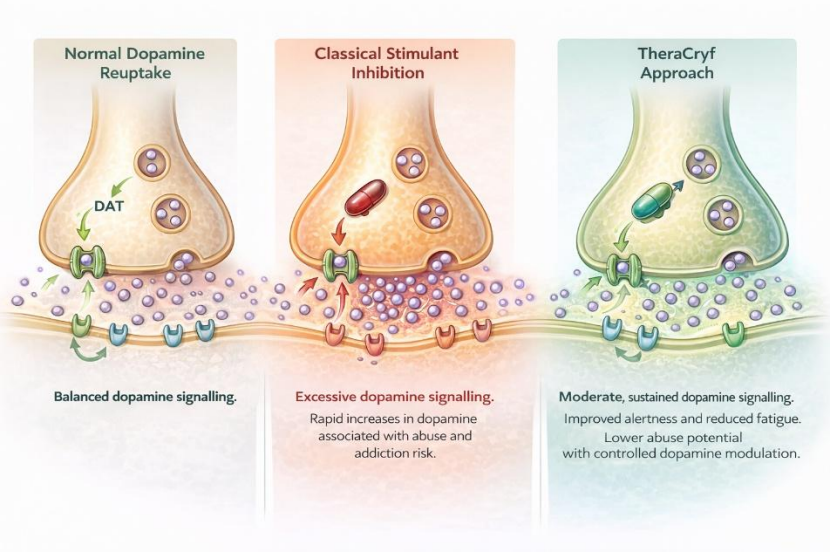
3. The orexin pathway is well characterised, with clinical validation established through dual orexin receptor antagonists (DORAs) in sleep disorders, and a substantial body of preclinical evidence demonstrating that selective Ox-1 antagonism can modulate reward-driven behaviour and reduce cue-induced relapse. This provides a supportive biological framework and partially de-risks the development of Ox-1-targeted therapies such as CT-010018.

4. TheraCryf defined a clear development pathway for CT-010018, with key milestones expected in 2026, including completion of IND/CTA-enabling studies, GMP manufacturing scale-up (already achieved) and progression towards first-in-human trials. Successful execution would represent a significant de-risking event and position the Company for potential licensing discussions with larger biopharma partners.

TheraCryf's DAT Programme

The second neurological product that TheraCryf is looking to develop is a brain dopamine transporter (DAT) inhibitor for generalised fatigue, secondary to a number of other conditions. DAT is a protein located in neurons within the brain which removes dopamine from the synapses and recycles it back in to the neuron. Inhibiting this process is hypothesized to increase dopamine signalling and increasing motivation and energy.

Figure 4: DAT inhibition in the brain



Source: Author illustration

TheraCryf's product is positioned as a candidate-stage atypical DAT inhibitor for both central fatigue and the orphan indication of narcolepsy. Preclinical proof-of-concept has been demonstrated across multiple animal models, including drug-induced fatigue, multiple sclerosis-related fatigue and narcolepsy. The aim is to deliver meaningful differentiation from classical dopamine-enhancing stimulants, which remain the current therapeutic standard (often used off-label), including methylphenidate (originally developed as Ritalin for ADHD by Ciba-Geigy, now part of Novartis), bupropion (originally developed as Wellbutrin for depression by Burroughs Wellcome, now part of GlaxoSmithKline) and modafinil (originally developed for narcolepsy by Lafon Laboratories and later commercialised by Cephalon, now part of Teva).

TheraCryf's candidate is designed to increase brain dopamine signalling in a more gradual manner, avoiding the rapid "peak" or "rush-like" profile associated with existing treatments and their potential for abuse. We do not expect significant near-term news flow from this programme, with management likely to prioritise the progression of CT-010018 through preclinical validation before allocating additional capital to secondary assets.

Fatigue & DAT

Generalised fatigue is rarely a single-disease entity. It can be driven by many factors, including multiple sclerosis (MS), myalgic encephalomyelitis (ME), chronic fatigue syndrome (CFS), long COVID, chemotherapy, sleep disorders, depression/anxiety, medications and inflammatory diseases. In practice, the current standard of care is multi-modal and generally involves ruling out and treating reversible contributors (e.g. sleep apnoea, anaemia, hypothyroidism, medication side-effects), before combining non-pharmacologic strategies (e.g. graded exercise/rehabilitation, cognitive behavioural therapy) with selective pharmaceutical interventions. It is a poorly defined market, but some estimates suggest that the total economic burden of fatigue-related conditions, including both treatment costs and lost productivity, exceeds USD100–150bn annually across major markets (e.g. ME/CFS, MS fatigue, cancer-related fatigue and long COVID), sourced from CDC, NIH and related health-economic analyses.

Fatigue is a prevalent and often debilitating symptom across a range of neurological and systemic conditions, with a significant impact on quality of life and functional productivity. While there has been considerable investigation into the pharmacological management of fatigue, treatment options remain limited and are frequently used off-label. For example, a randomised clinical trial published in The Lancet Neurology (Krupp et al., 2021 https://www.thelancet.com/journals/laneur/article/PIIS1474-4422(21)00243-3/fulltext) evaluated the use of amantadine (originally developed as an antiviral for influenza A), modafinil and methylphenidate in patients with multiple sclerosis-related fatigue, and found that none of these agents demonstrated a significant benefit over placebo, while all were associated with increased adverse events. Despite these limitations, such agents continue to be used in clinical practice, reflecting the lack of effective, well-tolerated therapies and highlighting a clear unmet need for novel approaches.

Narcolepsy represents a more clearly defined indication where pharmacological treatment has been successfully developed. Modafinil (Provigil) demonstrated efficacy in clinical trials and was approved by the FDA in 1998 for excessive daytime sleepiness associated with narcolepsy. Peak global sales of Provigil were approximately USD1.0–1.2bn prior to generic entry. Its successor, armodafinil (Nuvigil) from Cephalon, developed as the single optical isomer (R-enantiomer) with improved pharmacokinetics and tolerability, achieved peak sales of approximately USD0.5–0.7bn in the early 2010s. Both agents are also widely used off-label in broader fatigue-related conditions. Jazz Pharmaceuticals also was successful in the area, with its oxybate franchise (Xyrem and Xywave) seeing peak sales of over USD2bn, although its activity was more based around improved night-time sleep architecture than directly impacting wakefulness and motivation during the day. Despite the commercial success of both of these franchises, concerns regarding side effects, tolerance and abuse potential have persisted, suggesting a significant opportunity for novel therapies that can deliver sustained efficacy with improved safety and lower misuse risk.

We believe the most appropriate starting point for sizing the opportunity for TheraCryf's DAT inhibitor is within defined and clinically recognised indications such as multiple sclerosis-related fatigue. Approximately 70–80% of the ~2.8 million global MS population experience fatigue and a meaningful proportion are already treated with off-label pharmacological agents. On this basis, we estimate a core addressable market of approximately USD1–3bn. Beyond MS, fatigue represents a common and under-treated symptom across a range of conditions, including cancer, depression and long COVID, suggesting a broader opportunity over time. The commercial success of therapies in narcolepsy and hypersomnia, which collectively generate several billion dollars in annual revenues, further supports the willingness of payers to reimburse effective treatments targeting wakefulness and fatigue.

SFX-01 in GBM/neurology

History and oncology development

SFX-01 represents a legacy oncology asset based on a stabilised formulation of sulforaphane, a naturally derived compound with well-documented anti-proliferative and cytoprotective properties, including modulation of signalling pathways such as STAT3 and NF-κB that are implicated in tumour growth and resistance. The programme was originally developed by the Company with a focus on hormone-resistant breast cancer, supported by encouraging preclinical data suggesting an effect on cancer stem cells and treatment resistance. Whilst an open-label Phase 2 study demonstrated biological activity, it did not generate sufficiently robust efficacy to justify progression into larger, capital-intensive studies, particularly in the context of rapidly advancing standards of care with agents such as the CDK 4/6 inhibitors, including Ibrance from Pfizer.

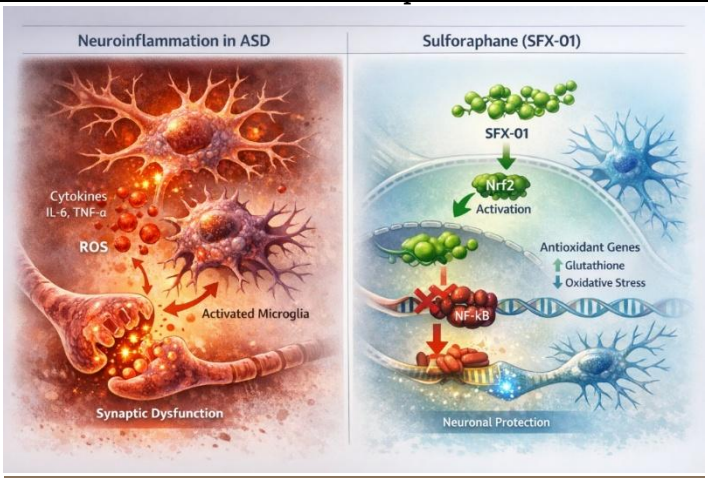
This outcome was a key factor underpinning the Company's subsequent strategic reset, with management electing to pivot away from internally funded oncology development and reallocate capital toward neuroscience, where development pathways are typically more capital-efficient and CT-010018 offers a clearer and more differentiated opportunity with nearer-term value inflection points. Despite this shift, SFX-01 has not been discontinued and continues to be explored in glioblastoma (GBM), an area of very high unmet need with limited effective therapies, as well as in neurodevelopmental disorders (NDDs), through academic and partner-led studies.

The continued development of SFX-01 in oncology is largely grant-funded (such as the work being undertaken at the Erasmus Medical Centre in Rotterdam looking at activity in GBM tissue samples), meaning that progress can be made with minimal capital allocation.

SFX-01 in neurological indications

In October 2022, TheraCryf licensed the global rights for SFX-01 in neurodevelopmental disorders (NDDs), such as autism spectrum disorder (ASD) and schizophrenia, to Stalicla, a private Swiss biotech company. Stalicla is funding clinical development activities, with TheraCryf retaining potential economic interest via milestones and licensing payments should the product be successful (of up to USD160m). The therapeutic rationale in neurodevelopmental disorders (NDDs) is driven by the relationship between these conditions and neuroinflammation/oxidative stress in certain patient sub-sets, the hypothesis being that sulforaphane can reduce these and create a therapeutic benefit. Recent literature increasingly supports both the inflammatory nature of certain NDDs and the ability of sulforaphane to exert anti-inflammatory and neuroprotective effects (via pathways including NRF2 activation and NF-κB inhibition).

Figure 5: Neuroinflammation in ASD and possible SFX-01 beneficial effects



Source: Author illustration

There are currently no available drugs indicated to impact the underlying mechanism of ASD. Products such as the anti-psychotics risperidone and aripiprazole are approved but they are to target the irritability that is often seen in ASD patients. ASD is mainly treated by individualised behavioural and educational intervention, occupational therapy, social skills supports and parent-mediated interventions. Whilst these can help, they do not treat the underlying disease causality and can be expensive and extremely time consuming, and if a therapeutic option became available to be used alongside these support mechanisms we believe it would be well accepted.

Stalicla positions STP2 (their codename for SFX-01) as a candidate for a biologically defined ASD subgroup ("Phenotype 2"), with a completed Phase 1 study currently being evaluated to support further development. The company is an NDD specialist, with its stated aim being to use AI to look at patient sub-groups and identify common disease signatures, matching these to potentially effective therapeutics (in this case with SFX-01). The company has raised over USD80m via both equity issuance and non-dilutive funding since its founding in 2017, most recently (June 2025) receiving CHF2m from Addex Therapeutics to continue the development of its three clinical assets, including SFX-01. In Stalicla's published pipeline they refer to SFX-01 as being an NRF2 agonist, tying up with the biology we discuss above. They also identify the total addressable market for a successful drug in this sub-section of ASD as greater than USD2bn. In October 2022 TheraCryf received an initial $0.5m licensing fee from Stalicla for the asset, and in February 2024 lodged a Notice of Dispute for an additional $0.5m, which it believes is owed after the completion of human volunteer Phase 1b studies. We understand that both sides are speaking amicably and we would hope for a resolution in due course.

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