TheraCryf plc

TheraCryf has received a conditional, non-binding, indicative proposal for the acquisition of its lead drug candidate, Orexin-1 ('Ox-1') and dopamine transporter '(DAT') programmes. While the Board chose to unanimously reject this undisclosed indicative offer on the basis that it did not reflect the value or future commercial potential of the asset and so was not in the best interests of shareholders, it nevertheless reflects industry recognition of the opportunity for the treatment of addiction presented by its highly differentiated selective orexin-1 receptor ('OX1R') antagonist (or 'blocker'), which is expected to be clinic ready before end-2026. Indeed, research into the Central Nervous System ('CNS') and Neurology sectors are a hot place right now, having dominated global pharmaceutical M&A in 2025, capturing deals valued at US$30.7 billion according to EY/IQVIA and overtaking oncology for the first time. Eli Lilly's (NYSE: LLY) even more recent (March 2026) US$7.8 billion acquisition of Centessa Pharmaceuticals plc (Nasdaq: CNTA) to access its promising orexin receptor 2 ('OX2R') agonist pipeline to target disorders like narcolepsy and excessive daytime sleepiness, also highlights rising confidence in the therapeutic potential of orexin modulating therapies. The fact that such a high value was attributed to cleminorexton upon delivery of Breakthrough Therapy Designation and 'potential best-in-class profile' following Phase 2a studies, provides meaningful precedence for the worth of Theracryf's Ox-1 composition-of-matter patents, which could multiply considerably should Theracryf successfully steer it through early clinical trials. The fact that the Ox-1 programme has remained on schedule and budget throughout, prospectively creating a new treatment for additive behaviours and wider 'cue-driven' motivation in the absence of sedation and excessive sleepiness, remains far from reflected in the Group's current valuation.

Non-binding proposal to acquire lead neuropsychiatry assets

Theracryf received a conditional, non-binding, indicative proposal to acquire its lead neuropsychiatry assets. These include its lead candidate, Ox-1, which recently advanced into late preclinical development aimed at behavioural brain disorders, with initial primary target indications of Binge Eating Disorder ('BED') and Alcohol Use Disorder ('AUD'). While the offer was rejected and discussions terminated, it remains uncertain as to whether an improved proposal might still be forthcoming, or whether other interested parties might emerge. Theracryf's Chief Executive Officer, Dr. Huw Jones, stated that "It is encouraging to note that our assets are receiving commercial attention", and went on to reaffirm that "We fully expect that our own asset value will be further enhanced by phase 1 clinical data in due course."

Big Pharma pursuing shift from neurodegeneration to psychiatry

Recent neuroscience and central nervous system ('CNS') related mergers and acquisitions ('M&A') appear to confirm that Big Pharma is willing to move away from speculative assets like tau or amyloid targeting (e.g., Alzheimer's) towards psychiatry (mood disorders, schizophrenia, etc.) as a surer route toward near-term revenue potential. This seems consistent with their preferred 'bolt-on' strategies, as opposed 'company-altering' transactions to fill specific pipeline gaps, while aiming for assets that fit with their existing behavioural, cognitive and emotional disorder product positioning.

Stock Data

Share Price:	0.23p
Market Cap.:	£4.93m
Shares in issue:	2,148.96m
52 week high/low:	0.30p/0.18p

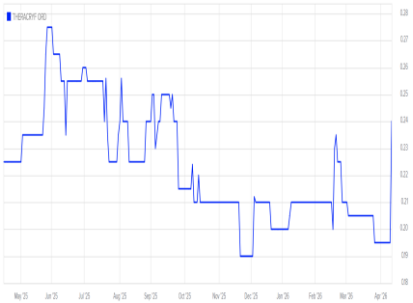
Company Profile

Sector:	Health Care
Ticker:	TCF
Exchange:	AIM

Activities

TheraCryf plc ('TCF', 'TheraCryf' 'the Group') is a clinical stage therapeutics company developing a new generation of innovative therapeutics in oncology and behavioural brain disorders.

1-year 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

Barry Gibb
Research Analyst

TPI acts as joint broker to TheraCryf plc.

Attention is drawn to the disclaimers and risk warnings at the end of this document.

In the past, neuroscience and CNS development had been hampered by difficulties in comprehending disease mechanisms and reaching targets across the blood-brain barrier. More recent advances in biomarkers (e.g., blood-based and digital diagnostics) and improved understanding of disease heterogeneity (segmenting patients more accurately) which, along with new delivery technologies, have reduced the risk profile for investors and developers. This is behind the recent spike in sector-related M&A activity detailed, for example, in EY's 2026 Firepower report which analysed the life sciences market, suggesting 2025 M&A activity surged to US$30.7 billion and outstripping traditional top-tier sectors like oncology. With focus on different psychiatric/neurological mechanisms, the industry is now also expressing greater confidence in the potential for orexin-modulating therapies, transitioning from primarily developing antagonists for insomnia to investing heavily in OX2R agonists for wakefulness disorders like narcolepsy. This shift has been driven by positive clinical data from players like Takeda and Alkermes, which are targeting the underlying root cause of the condition rather than just treating symptoms. In March 2026, Eli Lilly pushed this point home by announcing its US$7.8 billion acquisition of Centessa Pharmaceuticals (Nasdaq: CNTA), which is advancing its own OX2R agonist, ORX750, for narcolepsy ('NT1/NT2') and idiopathic hypersomnia ('IH'), with trials showing promising early data and a registrational program now underway. While Theracryf's Ox-1 is alternatively focused on inhibiting the OX1R receptor, confidence generated through recent clinical findings and the surge in related investment, clearly validates the orexin pathway and reduces perceived development risk.

Recent High Value Neuroscience and CNS M&A Transactions

Date	Acquiring Co.	Target Co.	Deal Value	Primary Asset / Focus	Indication
Mar-26	**Eli Lilly**	**Centessa Pharma**	**US$7.8B**	**Cleminorexton (OX2R agonist)**	**Sleep/Wake Disorders**
Feb-26	**Alkermes**	**Avadel Pharma**	**US$2.4B**	**ALKS 2680 (OX2R agonist) & LUMRYZ™**	**Narcolepsy /IH**
Jan-25	J&J	Intra-Cellular	US$14.6B	Caplyta (Lumateperone)	Psychiatry (Schizophrenia)
Oct-24	AbbVie	Aliada Thera.	US$1.4B	ALIA-1758	Alzheimer's Disease
Oct-24	Lundbeck	Longboard	US$2.6B	Bexicaserin (Epilepsy)	Epilepsy (Rare)
Aug-24	AbbVie	Cerevel Thera.	US$8.7B	Emraclidine (M4 agonist)	Psychiatry / Neurology
Mar-24	BMS	Karuna Thera.	US$14.0B	KarXT (M1/M4 agonist)	Psychiatry (Schizophrenia)
Jan-24	Bain Capital	Mitsubishi Tanabe	US$3.3B	Uplizna (Neurology)	Neurology (General)

Source: Market and Company data, TPI estimates

Orexins regulate arousal, sleep-wake cycles, feeding behaviour, reward and energy homeostasis

Orexin-based medications are poised for an increasingly significant future role due to their novel 'master switch' ability to regulate sleep, wakefulness, reward and other neurodegenerative diseases, moving beyond traditional sedatives or stimulants to offer more precise, tailored treatments for a wide range of neurological and psychiatric conditions. The orexin system effectively acts as a central conductor, making its modulation a 'blue sky opportunity' for such conditions.

Orexins, also known as hypocretins ('Hcrt'), are a pair of excitatory neuropeptides, namely Orexin-A (OxA/Hcrt-1) and Orexin-B (OxB/Hcrt-2), which are produced by a small population of neurons (c.50,000–80,000 in humans) in the lateral hypothalamus and perifornical area. Despite their limited number, these neurons project widely throughout the CNS to regulate arousal, sleep-wake cycles, feeding behaviour, reward and energy homeostasis. They also exert their effects by binding to two G-protein coupled receptors, OX1R and OX2R, as detailed overleaf.

These two receptors are distributed differentially in the brain, suggesting specialized roles. OX1R is highly expressed in the locus coeruleus (noradrenergic neurons), ventromedial hypothalamic nucleus, amygdalohippocampal area, and raphe nuclei. It is strongly linked to reward, emotion, and motivation. OX2R by contrast is primarily found in the tuberomammillary nucleus (histaminergic neurons), cerebral cortex, and hippocampus and is the dominant receptor for stabilising wakefulness. Both receptors are present in the ventral tegmental area and dorsal raphe.

Binding of orexins to their receptors typically leads to neuronal excitation, most frequently in terms of Gq Signalling, Ion Channels and Dimerization.

Comparison of Orexin Receptor Subtypes

Feature	OX1R	OX2R
Ligand Affinity	Orexin-A > Orexin-B	Orexin-A = Orexin-B
G-Protein	Gq/11	Gq/11, Gi/o
Major Role	Motivation, Reward, Emotion	Wakefulness, Sleep Stability
Key Location	Locus Coeruleus, Amygdala	Tuberomammillary Nucleus

Source: Academic papers, TPI estimates

The distinct therapeutic applications of each receptor, with OX1R recognised as a key target for behavioural/ metabolic conditions, plus potential for researchers to leverage their knowledge of the orexin system, suggests future focus will increasingly be on their independent (i.e. single orexin receptor antagonists or 'SORA'), rather than dual orexin receptor antagonists (or 'DORA') development. While suvorexant (Belsomra) and lemborexant (Dayvigo) were approved to treat insomnia by targeting OX1R and OX2R receptors to improve sleep initiation and maintenance, users have indicated that blocking both can sometimes induce or exacerbate symptoms such as cataplexy-like episodes and sleep fragmentation, rather than fully alleviating the conditions in all contexts. So, while nuanced approach to dual targeting may be assumed for enhancing arousal/treating hypersomnia, it appears selective targeting remains important for psychiatric and behavioural disorders. Note that in February 2026, the FDA accepted the New Drug Application ('NDA') and granted priority review for oveporexton (TAK-861) to treat narcolepsy type 1 ('NT1') by directly targeting the underlying orexin deficiency using just a potent OX2R agonist. In Phase 3 trials it significantly improved wakefulness and reduced cataplexy, demonstrating potential as a first-in-class and representing a further important move toward SORAs.

Comparison of FDA-Approved Dual Orexin Receptor Antagonists

Drug Name (Brand)	Developer	Mechanism	FDA Approval Date	Indication
Suvorexant (Belsomra)	Merck & Co.	Dual Orexin Receptor Antagonist (OX1R and OX2R)	August 13, 2014	Insomnia characterized by difficulties with sleep onset and/or sleep maintenance
Lemborexant (Dayvigo)	Eisai Co.	Dual Orexin Receptor Antagonist (OX1R and OX2R)	December 20, 2019	Insomnia characterized by difficulties with sleep onset and/or sleep maintenance
Daridorexant (Quviviq)	Idorsia Pharmaceuticals	Dual Orexin Receptor Antagonist (OX1R and OX2R)	January 7, 2022	Insomnia characterized by difficulties with sleep onset and/or sleep maintenance

Source: Market and Company data, TPI estimates

Ox-1 programme has demonstrated class-leading selectivity and high receptor occupancy

High selectivity (>100 fold) is considered critical for Ox-1 in order to permit the drug to specifically target addiction-related pathways while avoiding the side effects associated with inhibiting the orexin-2 receptor, including severe sedation or sleep disruption. By targeting only the Ox-1 receptor, the compound aims to treat daytime behaviours such as BED and AUD without affecting the normal sleep/wake cycle. This signals that the molecule has fully addressed issues that held back previous compounds (including a number of early GSK molecules) is particularly important, given that the side-effect profile of a drug often dictates its market viability.

In a 23 March 2026 update, TheraCryf reported that its Ox-1 blocker was well-tolerated at doses up to 1g/kg in regulatory toxicology studies. This is a critical indirect indicator of selectivity, given that if the drug had significant off-target binding to the OX2R at high concentrations, one would expect to see profound, dose-limiting sedation or

sleep-like states *in vivo*. The fact that the drug was well-tolerated at such high doses provides good evidence that it achieves a wide "therapeutic window" (a high margin between the desired OX1R effect and the unwanted OX2R one). It also successfully demonstrated ability to bind to (i.e., block) a large percentage of orexin-1 receptors in the brain. With strong target engagement, high drug potency and potential for improved efficacy, Ox-1 has become significantly derisked. Based on these results, doses were selected for its pivotal 28-day toxicology studies, which is the final major preclinical assessment. This is considered a near final step on the path to IND/CTA readiness and, having already commenced, final reporting is scheduled for Q3 2026.

Specific disclaimers

TPI acts as Joint Broker to Theracryf plc. ('Theracryf') which is listed on the AIM Market of the London Stock Exchange ('AIM').).

TPI as a business, its officers, private clients, or institutional clients may hold, subscribe for or buy or sell Theracryf securities. Opinions and estimates in this document are entirely those of TPI as part of its internal research activity. TPI has no authority whatsoever to make any representation or warranty on behalf of Theracryf.

General disclaimers

This document, which presents the views of TPI's research analyst, cannot be regarded as "investment research" in accordance with the FCA definition. The contents are based upon sources of information believed to be reliable but no warranty or representation, express or implied, is given as to their accuracy or completeness. Any opinion reflects TPI's judgement at the date of publication and neither TPI nor any of its directors or employees accepts any responsibility in respect of the information or recommendations contained herein which, moreover, are subject to change without notice. Any forecast or valuation given in this document is the theoretical result of a study of a range of possible outcomes and is not a forecast of a likely outcome or share price. TPI does not undertake to provide updates to any opinions or views expressed in this document. TPI accepts no liability whatsoever (in negligence or otherwise) for any loss howsoever arising from any use of this document or its contents or otherwise arising in connection with this document (except in respect of wilful default and to the extent that any such liability cannot be excluded by applicable law).

The information in this document is published solely for information purposes and is not to be construed as a solicitation or an offer to buy or sell any securities or related financial instruments. The material contained in the document is general information intended for recipients who understand the risks associated with equity investment in smaller companies. It does not constitute a personal recommendation as defined by the FCA or take into account the particular investment objectives, financial situation or needs of individual investors nor provide any indication as to whether an investment, a course of action or the associated risks are suitable for the recipient.

This document is approved and issued by TPI for publication only to UK persons who are authorised persons under the Financial Services and Markets Act 2000 and to professional clients, as defined by Directive 2004/39/EC as set out in the rules of the Financial Conduct Authority. This document may not be published, distributed or transmitted to persons in Japan, Canada or Australia. This document may not be copied or reproduced or re-distributed to any other person or organisation, in whole or in part, without TPI's prior written consent.

U.S. Persons Research Disclaimer

To the extent that any TPI research is furnished to U.S. recipients, it is furnished in reliance on Rule 15a-6 ("Rule 15a-6") under the U.S. Securities Exchange Act of 1934, as amended. The information contained in this research is intended solely for certain "major U.S. institutional investors" (as such term is defined in Rule 15a-6, an "MII") and may not be used or relied upon by any other person for any purpose. Each U.S. recipient of this research represents and agrees, by virtue of its acceptance thereof, that it is a MII and that it understands the risks involved in executing transactions in such securities. Any U.S. recipient of this research that wishes to discuss or receive additional information regarding any security mentioned herein, or engage in any transaction to purchase or sell or solicit or offer the purchase or sale of such securities, should contact a registered representative of Beech Hill Securities, Inc., a U.S. broker-dealer registered with the Securities and Exchange Commission and a Member of FINRA, located at 880 Third Avenue, 16th Floor, New York, NY 10022. Any transaction by a U.S. person (other than a registered U.S. broker-dealer or bank acting in a broker-dealer capacity) must be effected with or through Beech Hill Securities, Inc., which may be contacted via telephone at +1 (212) 350-7200.

This research was prepared by the analyst named on the cover of this research, who is a non-U.S. research analyst of TPI and, as such, may not be subject to all requirements applicable to U.S.-based analysts. All of the views expressed in this research accurately reflect the research analyst's personal view about all of the subject securities or research subjects and no part of such analyst's compensation was, is, or will be related to the specific recommendation or view contained in this research.

To the extent this research relates to non-U.S. securities, note that investing in non-U.S. securities may entail particular risks. Such securities may not be registered under the U.S. Securities Act of 1933, as amended, and the issuer of such securities may not be subject to U.S. reporting and/or other requirements. Financial statements included in research with respect to such securities, if any, may have been prepared in accordance with non-U.S. accounting standards that may not be comparable to the financial statements of U.S. companies. Available information regarding the issuers of such securities may be limited, and such issuers may not be subject to the same auditing and reporting standards as U.S. issuers. Fluctuations in the values of national currencies, as well as the potential for governmental restrictions on currency movements, can significantly erode principal and investment returns. Market rules, conventions and practices may differ from U.S. markets, adding to transaction costs or causing delays in the purchase or sale of such securities. Securities of some non- U.S. companies may not be as liquid as securities of comparable U.S. companies.

The information contained herein may include forward-looking statements within the meaning of U.S. federal securities laws that are subject to risks and uncertainties. Factors that could cause a company's actual results and financial condition to differ from expectations include, without limitation: political uncertainty, changes in general economic conditions that adversely affect the level of demand for the company's products or services, changes in foreign exchange markets, changes in international and domestic financial markets and in the competitive environment, and other factors relating to the foregoing. All forward-looking statements contained in this research are qualified in their entirety by this cautionary statement.

No TPI party accepts any liability whatsoever for any direct or consequential loss of any kind arising out of the use or reliance on the information given. Research does not take into account the specific investment objectives and financial situation of any recipient, nor do they provide individually tailored investment advice or offer tax, regulatory, accounting or legal advice. Prior to entering into any proposed transaction, recipients should determine, in consultation with their own investment, legal, tax, regulatory and accounting advisors, the economic risks and merits, as well as the legal, tax, regulatory and accounting characteristics and consequences, of the transaction. Investors seeking to buy or sell any financial instruments discussed or recommended in research, should seek independent financial advice relating thereto. The products discussed in research are not FDIC insured, may lose value and are not guaranteed by any TPI party.