SP ANGEL.

Healthcare research

Roquefort Therapeutics plc (To be renamed Coiled Therapeutics plc)

Ticker: ROQ LN (COIL LN post readmission)

Targeting solid tumours

Non-Independent Research

*SP Angel acts as Nomad and Broker to the Company

MiFID II Exempt

14 January 2026

Roquefort Therapeutics is executing an acquisition of the exclusive worldwide license for AO-252 for an upfront payment of £31.875m payable in shares together with a conditional placing of £10.5m (the "Placing"). Through this transaction, the new entity secures exclusive global rights to AO-252, a first-in-class small molecule targeting the TACC3 protein, now advancing into first-in-human studies for cancer treatment. The acquisition represents a decisive strategic pivot, expanding the pipeline to encompass both clinical and preclinical oncology programmes. With strong financial and operational backing from A2A Pharmaceuticals, Inc. ("A2A" or "A2A Pharma") and its investors, the combined entity is positioned to accelerate development and create meaningful shareholder value.

Acquisition of the AO-252 license

Roquefort Therapeutics has agreed to acquire an exclusive worldwide license for AO-252 from Coiled Therapeutics, Inc. ("Coiled USA") for £31.875m payable in shares. Coiled USA, a spin-out from A2A Pharma, holds exclusive worldwide rights to AO-252, a novel first-in-class drug targeting the TACC3 protein for cancer treatment. The Company also intends to progress Roquefort's STAT6 programme into Phase I. A2A and its investors are obliged to provide £3m in funding of the proposed £10.5m Placing. Before completion, Roquefort intends to carve out Lyramid Pty Ltd and the MK Cell programme for existing shareholders, and upon closing, the Company will be renamed Coiled Therapeutics plc and will be readmitted to trading on the AIM Market on the London Stock Exchange.

TACC3 inhibitor AO-252

AO-252 is an orally available, first-in-class small molecule that inhibits the TACC3 protein, which plays a critical role in cell division and is often overexpressed in aggressive cancers. By disrupting TACC3's protein-protein interactions, AO-252 induces mitotic & replication stress through impairment of DNA damage repair process and activating immunity leading to cancer cell death, particularly those with TP53 mutations, while showing minimal toxicity in healthy cells. AO-252 is currently in Phase I clinical trials in the US for advanced solid tumours, with early results demonstrating encouraging efficacy and a benign safety profile. TACC3 overexpression is linked to poor prognosis and increased aggressiveness in a wide range of cancers, making it a promising therapeutic target.

Phase I clinical trial

The Phase I clinical trial for AO-252 is an open-label, first-in-human study targeting advanced solid tumours, with a focus on patients who have TP53-mutated cancers. The trial consists of a dose-escalation phase to assess safety, tolerability, and pharmacokinetics, followed by an expansion cohort to further evaluate efficacy in additional tumour types. As of the latest update, 25 patients have been enrolled, and preliminary results show promising efficacy, including partial responses and tumour reductions, with no dose-limiting toxicities observed up to 240mg. The next phase will broaden enrolment to include more cancer types and aims to further characterize AO-252's therapeutic potential.

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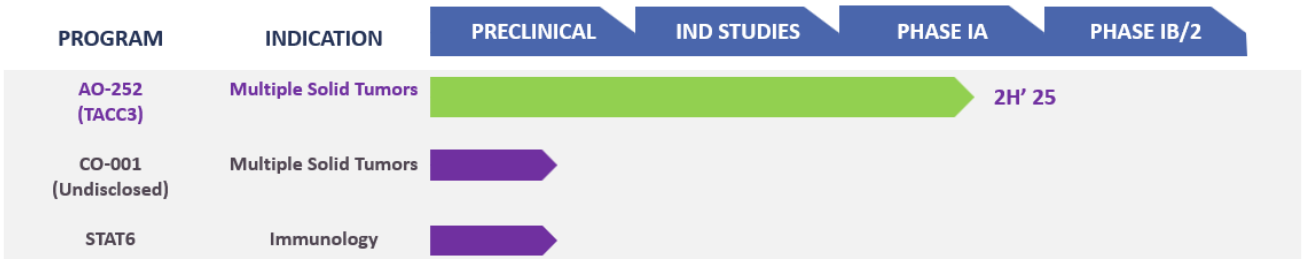
Executive summary

Roquefort Therapeutics to acquire the exclusive worldwide license for AO-252 from Coiled USA

Roquefort Therapeutics plc is undergoing a transformational acquisition of the exclusive worldwide license for AO-252 from Coiled USA, a spin-out from A2A Pharmaceuticals, Inc. for £31.875m *via* an all-share acquisition into Roquefort Therapeutics. Coiled USA holds exclusive global rights to AO-252, a first-in-class, first-in-human small molecule drug targeting the TACC3 protein for cancer treatment. As part of the proposed transaction, the Company will undergo the Placing to raise a minimum of £10.5m, with A2A obliged to cornerstone the Placing with an investment of £3m. This acquisition marks a strategic pivot for the company, expanding its pipeline to include both clinical and preclinical oncology programs, with a strong commitment from A2A and its investors to fund the merged entity. Upon completion, the name of the Company will be changed to Coiled Therapeutics plc.

Pipeline



Source: adapted from Coiled Therapeutics

Lead Asset: AO-252 (TACC3 Inhibitor)

AO-252 is a small molecule inhibitor of the TACC3 protein implicated in a number of aggressive cancers

AO-252 is an orally available small molecule designed to inhibit TACC3 protein-protein interactions, currently in Phase I clinical trials in the US for advanced solid tumours. The drug has shown encouraging efficacy and a benign safety profile in both preclinical and early clinical settings. The ongoing trial has expanded in Q4 2025 to include additional tumour types, with potential Phase II registrational trials to follow. The first prostate patient was enrolled in November 2025.

Scientific Rationale

TACC3 is a key regulator of cell division, and its overexpression is implicated in a wide range of aggressive cancers, including breast, lung, glioblastoma, bladder, and more. AO-252 disrupts TACC3's oncogenic functions, leading to mitotic & replication stress through impairment of DNA damage repair process and activating immunity, leading to cancer cell death, especially those with TP53 mutations. Preclinical studies demonstrate robust anti-tumour activity across multiple cancer models and minimal toxicity in healthy cells.

Pipeline Expansion

Beyond AO-252, Coiled intends to advance its STAT6 siRNA program, targeting immunology and oncology indications characterised by STAT6 overexpression. Preclinical results show a significant reduction in STAT6 expression and anti-cancer activity in validated models, supporting future clinical development.

Market Opportunity

The addressable market for AO-252 is substantial, with an estimated 150,000 patients in the US alone across various solid tumour types exhibiting TP53 mutation and high TACC3 expression. TACC3 overexpression is frequent and clinically significant, making it a promising biomarker and therapeutic target. The global solid tumour market is large and growing, driven by rising cancer incidence and the need for novel therapies.

Financials & Valuation

Industry benchmarks for Phase I oncology assets show median upfront licensing deal values of $67m, with total deal values reaching up to $1.3bn. Coiled's acquisition of AO-252 aligns with these valuations, reflecting its innovative, first-in-class status. Oncology remains the leading therapeutic area for dealmaking, with high interest from major pharmaceutical companies.

Key Milestones (2025–2027)

Key Milestones	
Complete dose escalation	Q1 2026
Initiate the dose expansion in other tumour types	Q1 2026
Initiate combination trials with standard-of-care	H1 2026
Identify indications of interest for further expansion	H2 2026
Present data for expansion	H2 2026
FDA discussion for registrational strategy	H1 2027

Investment thesis

Upon completion of the acquisition, the Company will be characterised by a strong blend of scientific, clinical, strategic, and financial capabilities, uniquely positioning it as an attractive investment opportunity.

From a pre-clinical to clinical stage company

Following the acquisition, Roquefort moves from a pre-clinical stage company to a clinical company

With this acquisition, Roquefort moves directly from a pre-clinical platform to a clinical-stage biotech company. It now has an active Phase I/II trial (NCT06136884) underway, which is already enrolling patients in the US. This provides short-term opportunities and makes the investment less risky compared to other companies still in the pre-clinical phase.

AO-252: first-in-class TACC3 inhibitor with a differentiated mechanism of action and broad application

AO-252 has the potential to be a first-in-class TACC3 inhibitor ...

AO-252 is an innovative oral small molecule designed to selectively disrupt cancer-critical protein-protein interactions involving TACC3, a target that is overexpressed in various aggressive malignancies but not required in normal cells. This mechanism of action may provide substantial efficacy with a favourable safety profile and reduced toxicity compared to chemotherapy or less selective targeted therapies. Notably, AO-252 can cross the blood-brain barrier and has shown preclinical evidence in multiple solid tumour models with complete tumour regression across multiple solid-tumour models, including ovarian, triple-negative breast, endometrial, gastric, prostate, and brain metastases.

Encouraging early clinical proof-of-concept data

... with encouraging early clinical benefit and safety profile

AO-252 has demonstrated a favourable safety profile in 24 enrolled patients and early signs of clinical benefit, including unconfirmed partial responses with tumour reductions of 29–33% lasting 6–8 months at sub-maximal exposures. Dose escalation continues, with completion expected in Q1 2026 and expansion cohorts planned also for Q1 2026, offering multiple near- and medium-term value inflexion points.

STAT-6 siRNA programme

In addition to developing AO-252 as a clinical asset, the Company plans to move forward with its unique STAT-6 siRNA programme, which is being prepared for an IND application and entry into Phase I trials targeting oncology and possibly immunology. By pursuing both assets, the Company aims to spread risk and stay focused on areas of high unmet need in oncology and potentially immunology.

Solid funding and aligned investors

A2A and its group of investors, who have a strong history of generating value (such as the 2018 spin-out and eventual $1bn peak valuation of Biomea Fusion), are providing a substantial portion of the necessary funding over the coming two years, including an obligation to invest £3m in the Placing. This major contribution lowers the risk of financing and ensures that experienced, long-term biotech investors share interests with Roquefort shareholders.

Experienced leadership team

Through its partnership with A2A Pharma and utilisation of the AI-driven SCULPT™ platform responsible for discovering AO-252, the Company leverages both expert teams and advanced technology with a proven track record of efficiently identifying and progressing first-in-class assets from initial concept to clinical development.

Strong oncology market

Due to its distinctive mechanism of action on the cell cycle, AO-252 may be applicable to a broad spectrum of solid tumours characterised by p53 overexpression, which affects approximately 50% to 70% of cases depending on cancer type. This indicates a substantial potential market within oncology. Demonstrated efficacy across numerous solid tumour models, along with the possibility for combination therapy, highlights considerable opportunities for label expansion and the ability to reach a significant patient population.

Coiled Therapeutics plc

The origin

Roquefort Therapeutics plc, has announced a planned transformational acquisition of an exclusive worldwide license for AO-252 from Coiled USA *via* an all-share acquisition for an upfront consideration of £31.875m, to be satisfied by issuing Ordinary Shares ("Consideration Shares") to Coiled USA's shareholders.

Roquefort Therapeutics plc

Roquefort was incorporated on 17 August 2020 as a public company limited and listed on the Main Market (as Roquefort Investments) on 22 March 2021, with the aim of acquiring businesses focused on early-stage opportunities in the medical biotechnology sector. Following this strategy, the Company made two key acquisitions:

- In December 2021, Roquefort made its first acquisition, Lyramid Limited, an Australian company that had an exclusive global licence for a patent portfolio covering Midkine antibodies, for an initial consideration of £1.0m. On 4 November 2025, the exclusive global licence for Midkine antibodies was terminated.
- In September 2022, Roquefort acquired the entire issued share capital of Oncogeni. This UK company had exclusive global licences for a patent portfolio covering novel MK Cell and siRNA STAT-6 programmes, in exchange for £5.5m.

In February 2025, Roquefort formalised the out-licensing of its MK Cell programme to Pleiades through its subsidiary Midkine Investments. The deal combines up to $25m in milestone payments with a perpetual 1.5% royalty on global net sales. Early milestones relate to Pleiades securing fundraising and progressing the asset into first-in-human studies, while the bulk of the value, $21m, is tied to commercial sales targets ranging from $10m to $300m.

Separately, the Company updated the status of the sale of its subsidiary Lyramid to Pleiades, a transaction worth up to $10.8m. Because Pleiades has not yet completed its fundraising with institutional and sovereign wealth fund investors in the GCC (Gulf Cooperation Council), the longstop date has been extended to 16 March 2026. The SPA has also been amended so that Midkine Investments, rather than Roquefort Therapeutics, is now the selling entity, and to acknowledge the scheduled termination of Lyramid's third-party licence to the Midkine antibody programme in November 2025.

Coiled Therapeutics plc

Coiled USA is a spin-out company from A2A Pharmaceuticals Inc.

Coiled USA is a spin-out company from A2A Pharma and holds the exclusive worldwide rights to its leading asset: AO-252. AO-252 is a novel first-in-class, first-in-human drug targeting the TACC3 protein for the treatment of various cancers, presenting a potentially less toxic approach compared to traditional chemotherapeutic treatments. The promise of this asset is highlighted by the success of a previous A2A Pharma spin-out, Biomea Fusion, a US-based clinical-stage diabetes and obesity medicines company focused on the development of two oral small molecules, icovamenib (Phase II trial) and BMF-650 (preclinical), which achieved a peak market capitalisation exceeding $1bn back in 2023 (now: $103m).

The drug, AO-252, is currently undergoing a Phase I clinical trial in the USA (clinicaltrials.gov ID: NCT06136884) for advanced solid tumours, where it has

shown encouraging efficacy, responses, and clinical benefit coupled with a very benign safety profile. This clinical data is supported by strong efficacy in preclinical models of multiple solid tumours. Coiled USA's clinical plan involves initiating dose expansion studies in the first quarter of 2026 and enrolling a sufficient number of patients throughout 2026 to pave the way for potential Phase II registrational trials, likely with a partner.

The transaction signals a clear strategic pivot for the acquiring company, which also intends to advance its existing STAT-6 programme currently in preclinical development into Phase I clinical trials *via* an Investigational New Drug (IND) application following key preclinical assays. A significant commitment to the merged entity's future is underscored by A2A Pharma and its investors, who have assured to provide the majority of the funding required over the next two years, with a £3m investment.

Upon the successful completion of the acquisition, the Company intends to change its name to Coiled Therapeutics plc (Ticker: COIL LN).

Transaction and financing details

The proposed transaction involves several key steps:

- Cancel its listing on the Main Market of the LSE.
- Apply for Admission to trading on the AIM market.
- Carry out an equity Placing to raise a minimum of £10.5 million, which is conditional on AIM Admission.

The initial consideration under the License Agreement payable to Coiled USA is £31,875,000, which will be satisfied by the issue of the Consideration Shares to the Coiled USA Shareholders on Admission.

The Company expects to undertake a 10:1 share consolidation in conjunction with the proposed transaction.

Deferred Consideration

Deferred Consideration Shares ("DCS") may be issued: Up to 75 million additional Ordinary Shares may be issued to A2A Pharma, assuming the share consolidation is approved, if the Company achieves market capitalisation targets of:

- £60m (25 million DCS);
- £90m (25 million DCS); and
- £120m (25 million DCS).

A2A Pharma and its introduced investors are obligated to cornerstone the Placing with a £3m investment.

License commercial terms

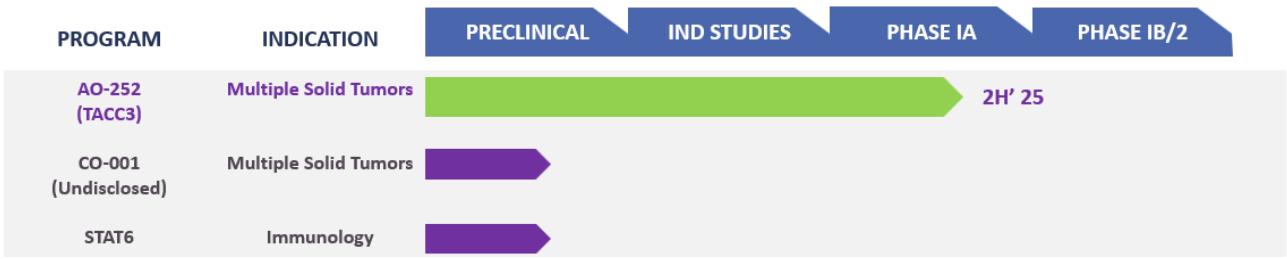
In addition to annual net sales royalties of up to 4%, the license includes potential cash milestone payments, such as:

- $1m for initiating Phase II;
- $5m for Phase III; and
- $6m for filing an NDA (New Drug Application) in the USA.

Pipeline

Coiled's projected pipeline consists of both clinical and preclinical oncology programmes. The main asset, AO-252, is currently undergoing a Phase I trial in the US targeting advanced solid tumours, where it is already demonstrating encouraging efficacy, positive responses, and clinical benefit, alongside a benign safety profile. In addition to AO-252, the Company intends to advance Roquefort's existing STAT-6 programme through the IND process into a Phase I clinical trial, further expanding its development pipeline.

Pipeline



Source: adapted from Coiled Therapeutics

Programme CO-001: Currently, the Company has not released specific information about this programme. However, it is understood that the initiative may involve next-generation AO-252 candidates or innovative modalities with a focus on targeting TACC3.

AO-252: a small molecule TACC3 inhibitor

AO-252 is a first-in-class, orally available small molecule designed to inhibit TACC3 protein-protein interaction, currently in Phase I trials for advanced solid tumours.

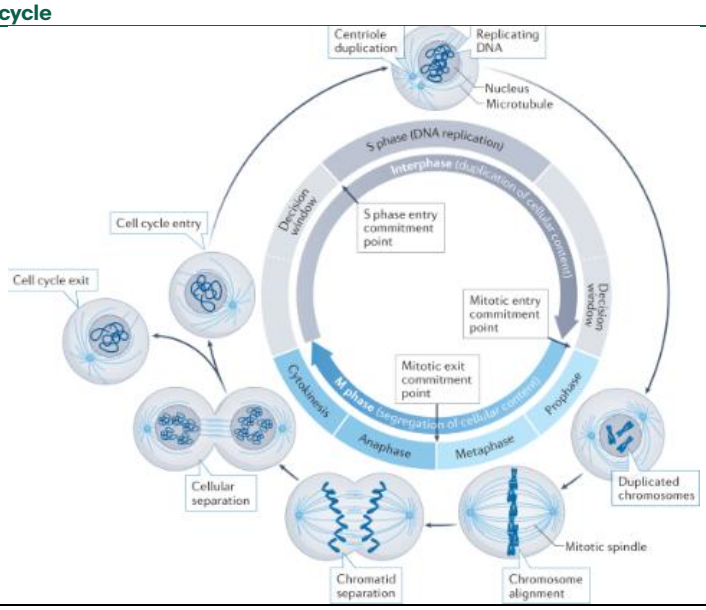
The TACC family of proteins

The TACC (Transforming Acidic Coiled-Coil) family of proteins is a small but highly conserved group of proteins found across various species, from yeast to humans, that are critical regulators of the cell division process. They are classified as centrosomal[1] and microtubule-associated proteins. Their specific location is dynamic and often depends on the phase of the cell cycle:

- **Centrosome/Spindle Poles:** This is their primary location, where they associate with the centrosome (the main microtubule-organising centre) and the spindle poles during cell division (mitosis).
- **Microtubules:** They directly interact with and bind to microtubules, the structural components of the mitotic spindle.
- **Nucleus/Cytoplasm:** Their concentration and precise location can shift, with components like TACC3 also found in the nucleus and cytoplasm during interphase. In the nucleus, TACC3 has been shown to interact with epigenetic regulators and DNA damage repair proteins, regulating cell cycle processes.

[1] A centrosome is a cellular structure involved in the process of cell division. Before cell division, the centrosome duplicates and then, as division begins, the two centrosomes move to opposite ends of the cell.

The cell cycle



Source: Nature, www.nature.com/articles/s41580-021-00404-3

Primary Function

The fundamental role of TACC proteins is to regulate microtubule dynamics and stability during mitosis (cell division). They accomplish this by acting as adaptor proteins in large complexes:

- **Spindle Stabilisation:** TACC proteins, particularly TACC3, are essential for assembling and stabilising the mitotic spindle, the structure that separates chromosomes. They work by recruiting other factors (like the microtubule polymerase and clathrin) to the spindle to create inter-microtubule bridges.
- **Genomic Integrity**: By ensuring the proper formation and function of the mitotic spindle, TACC proteins are crucial for accurate chromosome segregation, thereby maintaining genomic stability. Faulty TACC regulation can lead to aneuploidy (incorrect number of chromosomes) and cell death.

Significance

TACC family of proteins are implicated in several cases of cancer development and progression

The genes for TACC proteins are strongly implicated in disease, particularly cancer. Genetic alterations such as amplifications, mutations, or chromosomal translocations involving TACC genes have been observed in a range of malignancies. These genetic changes can lead to abnormal TACC protein expression or function, which disrupts normal mitotic processes and contributes to tumour development and progression. Consequently, TACC gene aberrations are not only markers of disease but are also considered potential therapeutic targets in oncology.

- **Oncogenic role**: TACC proteins are often found to be overexpressed or structurally rearranged (such as the fusion protein FGFR3-TACC3) in many types of aggressive cancers.

- **Cancer progression:** TACC overexpression can promote uncontrolled cell proliferation, enhance cell survival, and increase cancer aggressiveness by stabilising oncogenic signalling pathways and fuelling processes like aerobic glycolysis and epithelial-mesenchymal transition (EMT).

TACC3 protein

TACC3 is a highly dynamic protein whose primary function is to maintain the stability and proper assembly of the mitotic spindle. Its roles are precisely regulated across the cell cycle, and its dysregulation is highly relevant in oncology[2]. Its localisations in the cells are where the cellular division is taking place:

TACC3 protein plays a crucial role in microtubule stabilisation and chromosome segregation during cell division

- **Interphase** (when the cell is growing, replicates its chromosomes and prepares for cell division): TACC3 is mostly diffused in the cytoplasm and nucleus.
- **Mitosis** (replicated chromosomes are separated into two new nuclei): It rapidly concentrates and localises strongly at the centrosomes (spindle poles) and along the mitotic spindle microtubules. Its recruitment to the spindle is tightly regulated by phosphorylation.

TACC3 core function: microtubule stabilisation

During mitosis, TACC3 collaborates with other proteins to form a trimeric complex that is crucial for the proper assembly and stabilisation of the mitotic spindle. This complex includes TACC3 itself, the microtubule polymerase ch-TOG, and the clathrin heavy chain. TACC3 acts as an adaptor, bringing together ch-TOG and clathrin at the spindle, thereby facilitating the formation of robust, stable microtubule bundles necessary for accurate chromosome segregation.

Component	Role	Outcome
TACC3 (Adaptor)	Recruits and bridges other components.	Ensures proper spindle geometry.
Ch-TOG (Microtubule polymerase)	Promotes microtubule growth and polymerisation.	Creates stable microtubule connections.
Clathrin (Heavy chain)	Stabilises the TACC3/ch-TOG complex and acts as an inter-microtubule "bridge."	Maintains tension and structural integrity of the kinetochore fibres.

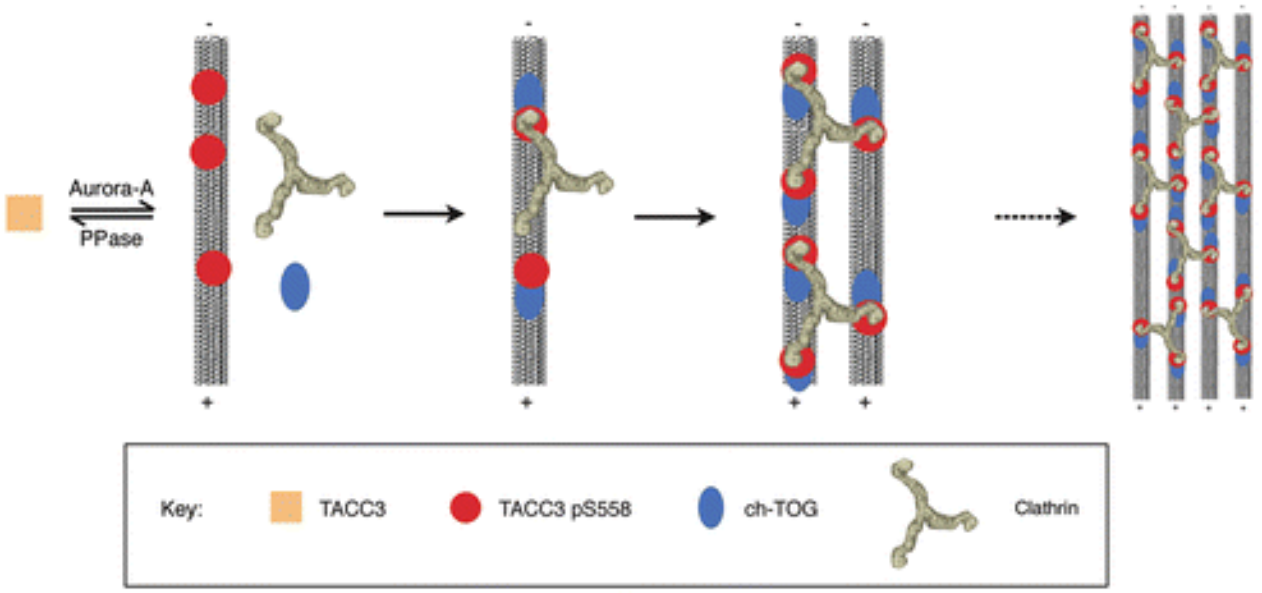
Source: Daniel G. Booth et al, A TACC3/ch-TOG/clathrin complex stabilises kinetochore fibres by inter-microtubule bridging, EMBO Journal, 2011, 30/906-19.

This TACC3/ch-TOG/clathrin complex functions as a molecular "bridge" between the microtubules that emanate from opposite poles of the spindle.

The figure below depicts the phosphorylation of TACC3 by Aurora A kinase enables it to bind to microtubules, where it can recruit clathrin and ch-TOG. Clathrin triskelia could interact with multiple TACC3 molecules on microtubules, including those on adjacent microtubules, in which case a bridge would be formed. Ultimately, many bridges would form between closely located microtubules, helping to stabilise microtubule bundles in kinetochore fibres. As the multiple contacts form in these complexes, all the individual components would interact more stably with the spindle.

[2] Holly Briggs, Euan S. Polson et al, The cell cycle state defines TACC3 as a regulator gene in glioblastoma, BioRxiv, 2020. https://doi.org/10.1101/2020.10.20.346643

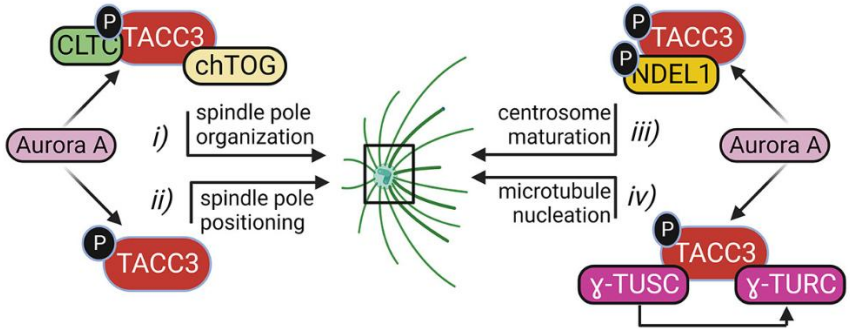
Model of recruitment and inter-microtubule cross-linking by TACC3/ch-TOG/clathrin complex



Source Hood, F. E., & Royle, S. J. (2011). Pulling it together: The mitotic function of TACC3. BioArchitecture, 1(3), 105–109. https://doi.org/10.4161/bioa.1.3.16518

This action is vital for creating the necessary tension on the chromosomes, ensuring they are correctly aligned and accurately pulled apart during cell division.[3] The following graph shows that TACC3 controls spindle pole organisation by interacting with clathrin (CLTC) and chTOG (i), and it also mediates spindle pole position (ii) under the control of Aurora A. TACC3 in complex with NDEL1 regulates centrosome maturation (iii), and TACC3 triggers microtubule nucleation by controlling the assembly of γ-TuRC from γ-TuSC (iv) under the control of Aurora A.

The functions of TACC3 and its interaction partners on the centrosomes



Source: Saatci, O., & Sahin, O. (2023). TACC3: a multi-functional protein promoting cancer cell survival and aggressiveness. *Cell Cycle*, *22*(23–24), 2637–2655. https://doi.org/10.1080/15384101.2024.2302243

TACC3's role in Cancer

Dysregulation of TACC3 protein leads to cancer development, cancer progression and cancer aggressiveness

TACC3 is a central player in cellular housekeeping, but when its regulation fails, it becomes a powerful driver of tumour growth, primarily by disrupting the mitotic process and participating in powerful oncogenic fusions. TACC3 is heavily implicated in cancer, often behaving as an oncogene (a gene that, when mutated or overexpressed, contributes to the conversion of a normal cell into a cancer cell)[4].

[3] Ryoji Yao et al. TACC3 is required for the proper mitosis of sclerotome mesenchymal cells during formation of the axial skeleton, Cancer Sci. 2007, 555-562.
[4] Congran Zhao et al. Downregulation of TACC3 inhibits tumor growth and migration in osteosarcoma cells through regulation of the NF-κB signaling pathway, 2018. www.spandidos-publications.com/10.3892/ol.2018.8262#:~:text=2C).,role%20in%20progression%20of%20osteosarcoma.

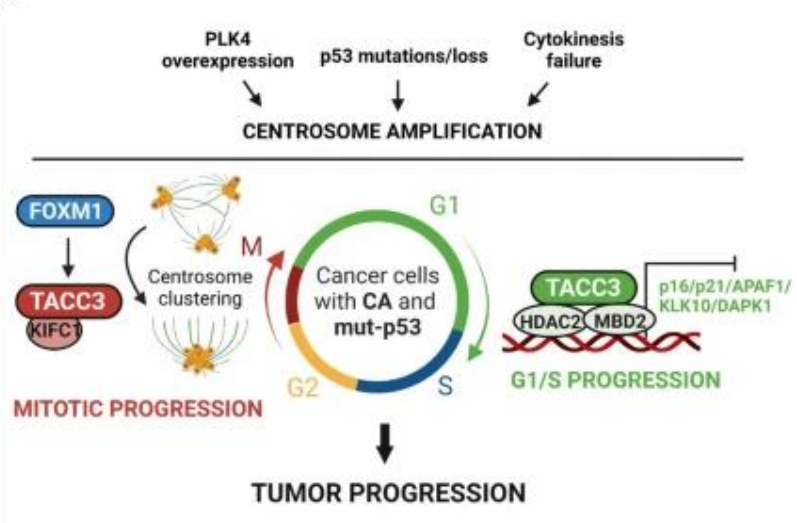
Over-expression and genomic instability

Its dysregulation and overstimulation lead to a cascade of cellular events, including the disruption of normal mitotic processes and the promotion of genomic instability. These alterations enable cells to evade standard growth controls and contribute to the malignant transformation and progression characteristic of tumours.

- **Aneuploidy driver** (abnormal number of chromosomes): TACC3 is frequently overexpressed in a wide range of human cancers (e.g., breast, gastric, colorectal, and glioblastoma). This excessive amount of TACC3 can lead to hyper-stabilisation of the mitotic spindle, resulting in faulty cell division and aneuploidy[5]. Genomic instability is a hallmark of aggressive tumours.
- **Promotes aggressiveness:** High TACC3 expression is directly correlated with poor prognosis, increased cell proliferation, enhanced invasion, and metastasis in many malignancies.

In cancer cells with centrome amplification that can be induced upon PLK4 overexpression, p53 modulation or cytokinesis failure, TACC3 is overexpressed and mediates distinct mitosis and interphase-specific functions to promote cell cycle and tumour progression. Mitotic TACC3 interacts with KIFC1 at the centrosomes and promotes centrome clustering to ensure mitotic progression and inhibition of apoptosis[6]. In addition, interphase TACC3 interacts with MBD2 and HDAC2, belonging to the nucleosome remodelling and deacetylase (NuRD) complex, to suppress the transcription of tumour suppressors (i.e., p16, p21, APAF1, KLK10 and DAPK1) and facilitate G1/S progression and cell survival.

TACC3 and tumour progression



Source: Ozge Saatci et al. Cell Death & Differentiation, 2023, 30, 1305-1319.

TACC3 and cancer aggressiveness

TACC3 overexpression has been observed in a wide and aggressive spectrum of solid tumours. Its increased expression is generally considered an unfavourable prognostic factor, correlating with worse overall survival and more aggressive disease characteristics.

[5] Faye M. Nixon et al., The mesh is a network of microtubule connectors that stabilizes individual kinetochore fibers of the mitotic spindle, Cell Biology, 2015. https://doi.org/10.7554/eLife.07635

[6] Ozge Saatci et al. Targeting TACC3 represents a novel vulnerability in highly aggressive breast cancers with centrome amplification. Cell Death & Differentiation, 2023, 30, 1305-1319.

Cancer type	Key findings and clinical evidence
Breast cancer	Highly expressed, particularly in aggressive subtypes like HER2-positive and triple-negative breast cancer. High TACC3 often correlates with centrosome amplification (a common feature of aggressive tumours) and is linked to poor survival.
Lung cancer	Specifically, high expression is observed in non-small cell lung cancer and is strongly associated with poor overall survival.
Glioblastoma	A highly aggressive brain tumour where TACC3 is upregulated, contributing to cell proliferation and tumorigenesis.
Bladder cancer	TACC3 overexpression is noted, but it is also a site for the clinically important FGFR3-TACC3 gene fusion.
Hepatocellular carcinoma	One of the most common liver cancers, where TACC3 is overexpressed and linked to a worse prognosis.
Gastrointestinal cancers	Overexpression is frequently reported in several digestive system cancers, including colorectal cancer, gastric cancer, oesophageal squamous cell carcinoma, and cholangiocarcinoma (CCA).
Ovarian cancer	Upregulation has been found and is associated with progression and poor outcomes.
Prostate cancer	High expression is linked to tumour progression and a poorer prognosis.
Renal cell carcinoma	Studies show that TACC3 knockdown can inhibit proliferation and invasion of RCC cells, indicating high expression drives disease.
Multiple myeloma	TACC3 is upregulated in this haematological malignancy.
Head and neck cancers	The FGFR3-TACC3 fusion has been identified in a subset of these cancers, highlighting a targetable molecular mechanism.

Source: SP Angel

The table above illustrates that targeting TACC3 with an inhibitor holds promise in addressing a wide spectrum of solid tumours. Given the protein's involvement in tumour progression and poor prognosis across multiple cancer types, inhibiting TACC3 could potentially disrupt critical oncogenic pathways. Whether administered as a single agent or in combination with other therapies, such an approach may enhance treatment efficacy and provide broader therapeutic options for patients affected by these malignancies.

AO-252, first-in-class TACC3 PPI inhibitor

Background

AO-252 is an orally available small molecule that selectively disrupts the interaction of the TACC3 protein with its other protein partners. It was initially developed jointly by A2A Pharma and OncoCube, with A2A Pharma subsequently licensing in OncoCube's 50% interest in June 2022 so that it then held a 100% interest. A2A spun off the project into Special Purpose Vehicle Coiled USA for further preclinical and clinical development.

While the exact structure of AO-252 is being kept undisclosed, the molecule is derived from the less bioavailable molecule BO-264. Its development has been published in two recent papers[7],[8] and four patents (Patent Family 1, including BO-264, granted, US 11622966 B2; Patent Family 2, pending US 2023/0027854 A1; Patent Family 3, pending, US 2024/0374590 A1; and Patent Family 4, granted, US 11986475 B1).

[7] Ozge Akbulut et al. A Highly Potent TACC3 Inhibitor as a Novel Anticancer Drug Candidate. *Mol Cancer Ther* 1 June 2020; 19 (6): 1243–1254. https://doi.org/10.1158/1535-7163.MCT-19-0957

[8] Deniz Lengerli et al. Isoxazole-pyrimidine derivatives as TACC3 inhibitors: a novel modality to targeted cancer therapy. Bioorganic Chemistry, March 2025, 156, 108204. https://doi.org/10.1016/j.bioorg.2025.108204

Strategic derivations and modifications have led to improved pharmacokinetic properties and enhanced therapeutic potential, distinguishing AO-252 from its predecessor and supporting its advancement into clinical evaluation.

AO-252: Mechanism of action

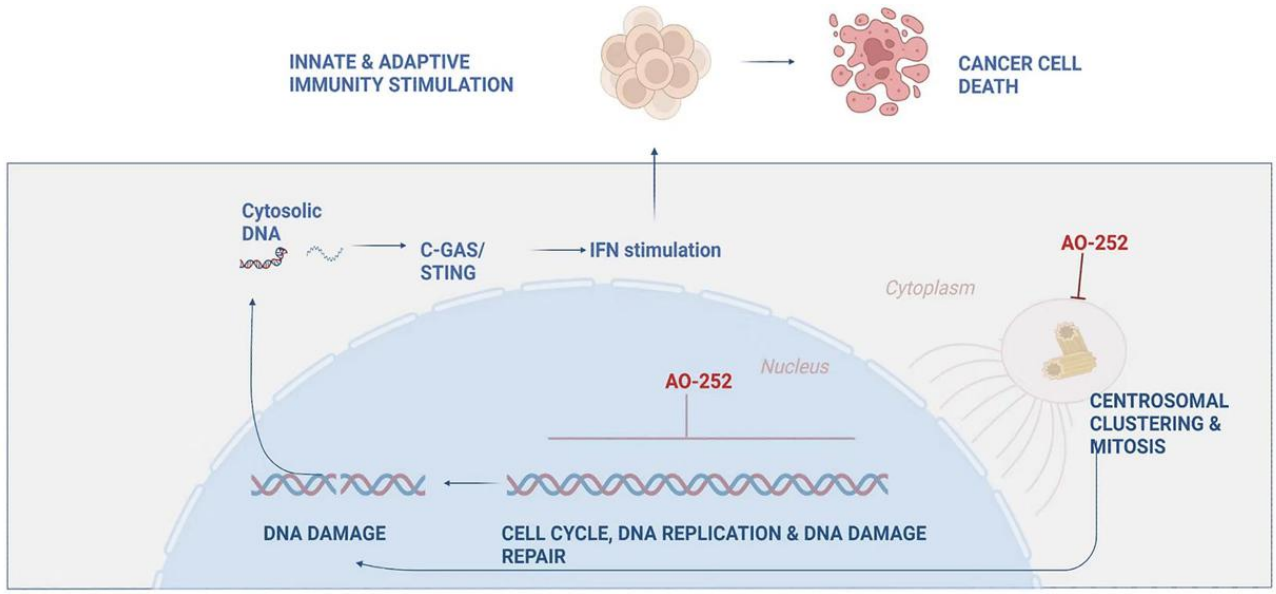
AO-252 is an orally available small molecule inhibiting selectively the interaction of the TACC3 protein with its binding protein partners

For instance, TACC3 plays a central role in ensuring proper spindle assembly during cell division, and its overexpression can drive abnormal mitotic events, resulting in aneuploidy and genomic instability, both hallmarks of cancer progression. In addition, TACC3's involvement in epigenetic regulation and gene transcription can lead to altered expression of oncogenes and tumour suppressor genes, further fostering an environment conducive to tumour growth and resistance to therapy. Its influence on immune modulation also suggests that TACC3 may help tumours evade immune surveillance, compounding its impact on malignancy. Collectively, these multifaceted functions make TACC3 a compelling therapeutic target, especially in cancers where its activity is heightened and closely linked to adverse clinical outcomes.

The mechanism of action centres on disrupting the oncogenic functions of TACC3. AO-252 selectively interferes with TACC3's binding to key partners such as Clathrin/KIFC1, BRD4, and MBD2/HAT complexes. These interactions are critical for TACC3's role in maintaining mitotic integrity and regulating epigenetic transcription.

By blocking these interactions, AO-252 induces mitotic stress, impairs DNA damage repair, and promotes apoptosis in cancer cells, particularly those with TP53 mutations, which are more vulnerable to chromosomal instability.

AO-252 mechanism of action



Source Company presentation:

AO-252 was evaluated *in vitro* across a panel of 242 tumour-derived cell lines to assess its effects on cellular proliferation. The distribution of cell lines included lung (68), breast (35), colon (29), ovarian (25), brain (20), bladder (16), endometrial/uterine (12), head and neck (11), gastroesophageal (14), cervical (6), and prostate (6). The median cellular efficacy measure EC50 observed was 50nM. Of the total lines tested, 39 (approximately 16%) exhibited less than 50% inhibition of proliferation at 5μM, representing various tissue origins. A correlation was identified between susceptibility to AO-252 and elevated TACC3 and centrome

amplification levels, with increased TACC3 expression associated with lower EC50 values, indicating enhanced efficacy.

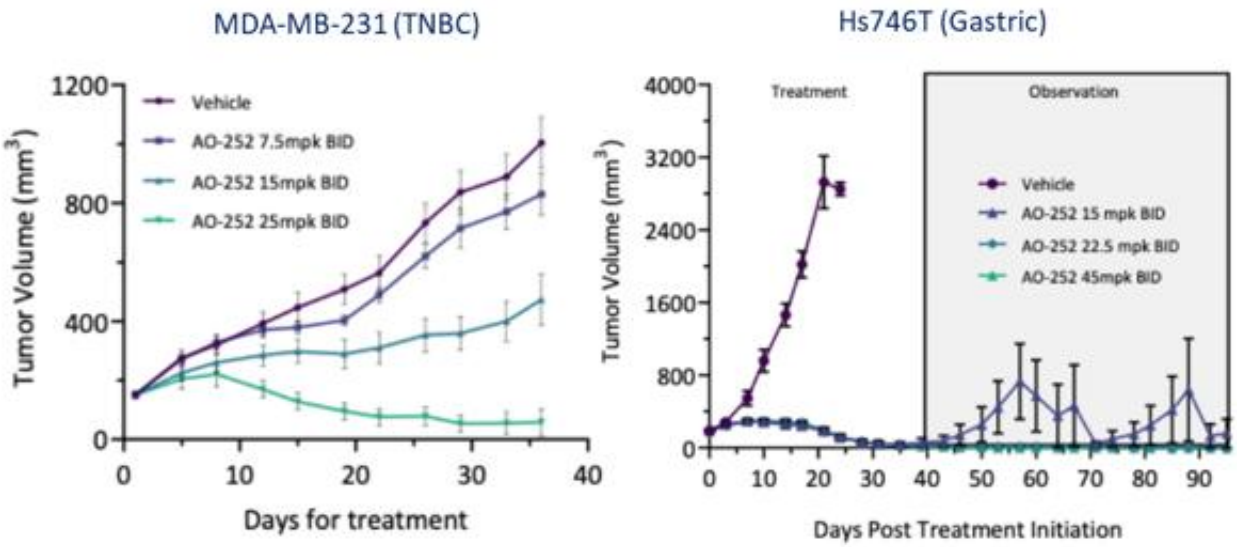
Importantly, assessment in normal cells indicated minimal toxicity, as evidenced by an EC50 of 3μM for human peripheral blood monocytes and greater than 30μM for liver hepatocytes.

Preclinical findings

Preclinical findings have demonstrated that AO-252 exhibits robust anti-tumour activity across a spectrum of cancer models. AO-252 has been tested in a number of cell-based assays and animal models. Partial or complete response was seen in several solid tumour models in a dose-dependent manner, including:

- triple negative breast cancer
- ovarian cancer
- prostate cancer
- endometrial cancer
- lung cancer
- bladder cancer
- oesophageal cancer
- gastric cancers.

***In vivo* effect of AO252 in triple-negative breast cancer and gastric cancer**



Source Company data

These results underscore the broad therapeutic potential of AO-252 and support its continued development for the treatment of diverse malignancies.

Safety profile

Importantly, AO-252 has demonstrated a favourable safety profile in preclinical studies, showing minimal impact on healthy cells at therapeutic doses. Nonetheless, as with many cancer agents, some side effects have been observed in animal models at high doses of AO-252, although these were generally manageable, species-related and consistent with expectations for this class of compounds.

- Histopathology data showed effects on testes/ovaries in the medium- and high-dose groups in rats and high-dose group in dogs. The observed impact appears to diminish progressively following the discontinuation of dosing.
- Reticulocyte counts fell in dogs given high doses, but recovered when dosing was lowered. This common risk with oncology drugs may be managed using erythropoietin, iron infusions, or colony-stimulating factors like G-CSF.

- Some cases showed a decrease in neutrophils and lymphocytes, which can lower the body's capacity to combat infections. It is important to monitor for fever. This effect often occurs with cancer chemotherapy and is managed using filgrastim injections (such as Neupogen®).
- Gastrointestinal tract toxicity was noted in non-GLP studies at high doses, which may be species-related. Vomiting and nausea can be managed with medications like ondansetron (Zofron®) or metoclopramide (Maxolon®).

IND submission & approval

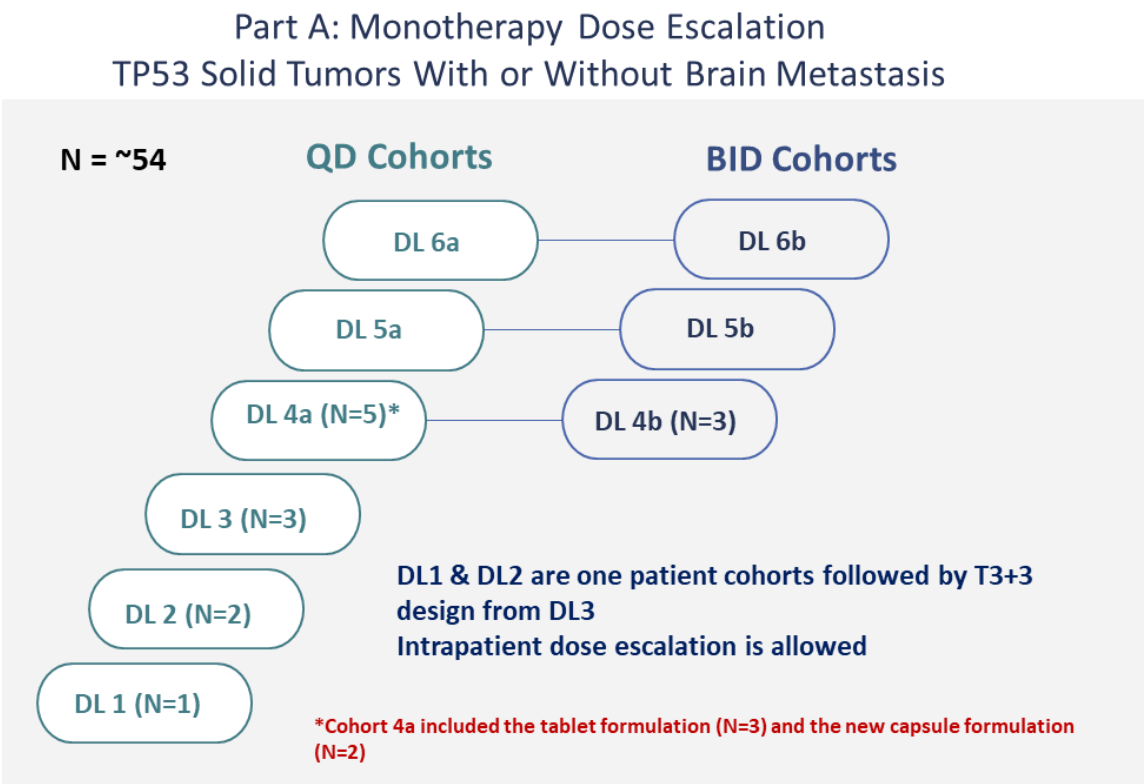
Following the data package from studies described above, the Investigational New Drug (IND) application for AO-252 was approved in May 2023 by the FDA. This regulatory milestone enables the initiation of first-in-human clinical investigations to further assess the safety and efficacy of AO-252 in patients with various solid cancer types.

Current status: Phase I clinical trial

Description

Coiled initiated the first-in-human trial with AO-252 in patients with advanced solid tumours, initially focused on TP53-mutated ovarian, endometrial and triple-negative breast cancers, and subsequently expanded (September 2025 protocol amendment) to all solid tumours, including patients with brain metastases. The Phase I is an open-label, clinical trial with AO-252 as a monotherapy under the clinicaltrials.gov ID NCT06136884.

Phase I clinical study



Source Company data

The study is expected to enrol ca.54 patients in the dose escalation study followed by a dose expansion, and is composed of two parts:

1. An initial dose-escalation phase to evaluate safety, tolerability, and pharmacokinetics of AO-252 in patients with advanced solid tumours with TP53-mutated ovarian, endometrial and triple-negative breast cancers.

2. Expansion cohort in 30-40 patients to further characterise efficacy signals in selected other tumour types. This trial aims to establish the recommended Phase II dose and further assess the therapeutic potential of AO-252 in a clinical setting.

The first study is designed with two arms: the first cohort receives the therapeutic drug once daily, while the second receives the drug twice daily.

Primary endpoints	Secondary & exploratory endpoints
Safety	Pharmacokinetics
Tolerability	Pharmacodynamics
	Response rate (RECIST 1.1)
	Duration of response
	Progression-free survival
	Overall survival

Source: Coiled Therapeutics

Ongoing Phase I trial – Efficacy to date

The dose-escalation study is currently underway at five sites across the United States, and to date, 24 patients have been enrolled, all diagnosed with triple-negative breast cancer, ovarian, or endometrial cancers. The dosing regimen involves once-daily escalation from 20mg to 240mg, as well as an 80mg twice-daily schedule.

To date, the Company observes encouraging preliminary efficacy:

- 33% partial response in an endometrial cancer patient (the cancer has shrunk significantly, but not completely disappeared) in the 80mg BID cohort.
- 29% ovarian tumour reduction in two patients in the 80mg BID cohort.
- No dose-limiting toxicities up to 120 mg BID (240mg/day).
- The BID (twice daily) dosing arm results in higher drug exposure than once daily.
- Mild-grade adverse events have been noted in some patients.

Adverse events profile

Adverse Event	Cohort 5b (Tablets) (N=3)			Cohort 4b (Tablets) (N=3)			Cohort 4a (Tablets & Capsules) (N=6)			Cohorts 1-3 (Tablets) (N=10)		
	Gr 1	Gr 2	≥Gr 3	Gr 1	Gr 2	≥Gr 3	Gr 1	Gr 2	≥Gr 3	Gr 1	Gr 2	Gr 3
Anemia	-	-	-	-	1[%]	-	-	-	-	1	-	-
Vomiting	-	-	-	-	-	-	-	-	-	1	-	-
Fatigue	-	-	-	-	-	-	1	-	-	1	-	-
ALT elevation	-	-	-	-	-	-	-	-	1*	-	-	-
AST elevation	-	-	-	-	-	-	-	1*	-	-	-	-
Hyperbilirubinemia	-	-	-	2[$]	-	-	1[$]	-	-	-	-	-
Brain Fog	-	-	-	1	-	-	-	-	-	1	-	-
Emotional lability	-	-	-	1	-	-	-	-	-	-	-	-
Anorexia	-	-	-	-	-	-	-	-	-	1	-	
Thrombocytopenia	-	-	-	1[&]	-	-	-	-	-	-	-	-
Weakness	-	1		-	-	1[&]	1[&]	-	-	-	-	-
Loss of appetite	1	1										

Source Company data

Importantly, drug exposure in the most recent cohorts remains below levels associated with maximal preclinical efficacy, indicating further upside as dose escalation continues. Dose escalation is on track for completion in Q1 2026.

The Company is preparing to initiate the monotherapy dose expansion phase, scheduled to commence in Q1 2026. This next stage will broaden enrolment to include patients with prostate, gastric, sarcoma, and brain metastases, in addition to the current indications. The expansion aims to further characterise AO-252's therapeutic potential across a wider spectrum of solid tumours.

Potential for combination studies

As with many cancer drugs, and due to its broad mechanism of action, there is a potential for AO-252 to be combined with an additional anticancer agent. Combination strategies may be explored to enhance efficacy, overcome resistance mechanisms, or mitigate adverse effects associated with monotherapy. Early preclinical data and the ongoing clinical trial may help identify rational partners for combination, such as immune checkpoint inhibitors or other targeted therapies, depending on the tumour type and molecular profile.

AO-252 has shown strong synergy in preclinical models when combined with established chemotherapy and targeted agents, including Enehrtu (trastuzumab deruxtecan), anti-PD-1 checkpoint inhibitors, and Trop2 antibody-drug conjugates. These findings provide a compelling basis for future combination

strategies aimed at enhancing efficacy and overcoming resistance mechanisms in solid tumours.

These promising preclinical findings support the rationale for future combination studies and may pave the way for expanded therapeutic options in solid tumours, particularly in patient populations where monotherapy is insufficient. Such options could be explored in Phase II/III studies.

Competition

To our knowledge, based on the most recent publicly available data, the clinical landscape for direct TACC3 inhibitors remains very narrow. With AO-252 being the only inhibitor currently in the clinic, Coiled Therapeutics is at the forefront of TACC3-targeted therapy development and underscores its potential significance within the oncology field. Being first-in-class development leads to a certain number of advantages, such as first for potential commercialisation, recognition from peers and higher potential for licensing/partnership. While the initial results for AO-252 are promising, several challenges may arise as the programme progresses. These could include patient recruitment difficulties for some tumour types, unforeseen safety signals at higher doses, or variability in response across diverse cancer subtypes. Furthermore, the complexities of designing combination studies and the potential for drug-drug interactions may present additional hurdles that require careful consideration and robust risk mitigation strategies.

In comparison, there are a number of companies that are developing Aurora A inhibitors, an upstream protein in the signalling pathway of TACC3. The most advanced is Takeda, with Alisertib that reached Phase III trials. While this upstream intervention may offer certain mechanistic advantages, it is often associated with a higher likelihood of off-target effects and broader toxicity profiles. This is because upstream kinases typically regulate multiple cellular processes, increasing the risk of unintended consequences and adverse events for patients.

Key catalysts:

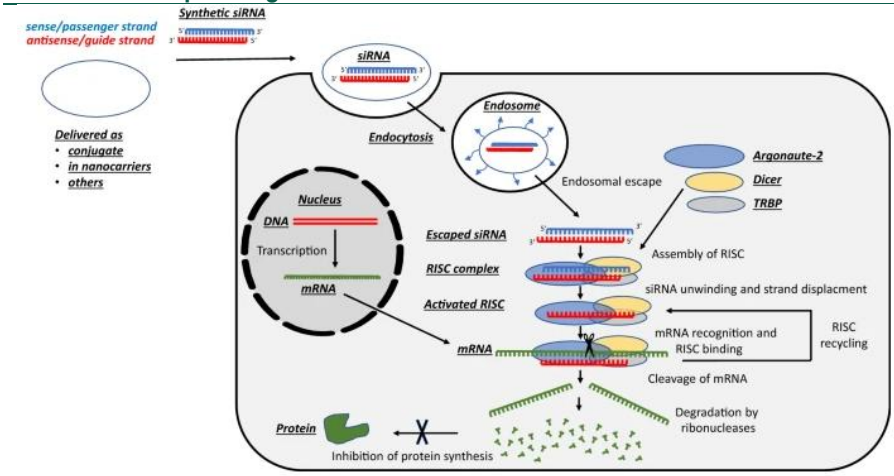
Complete dose escalation	Q1 2026
Initiate the dose expansion in other tumour types	Q1 2026
Initiate combination trials with standard-of-care	H1 2026
Identify indications of interest for further expansion	H2 2026
Present data for expansion	H2 2026
FDA discussion for registrational strategy	H1 2027

SiRNA STAT-6 inhibitors

Gene silencing as a therapeutic agent

In a very simple explanation, RNA interference is a natural biological process whereby small pieces of RNA (siRNA) inhibit protein translation by binding and degrading specific sequences of mRNA. Degradation of mRNA subsequently inhibits expression of the target proteins.

SiRNA as a therapeutic agent – Mechanism of action



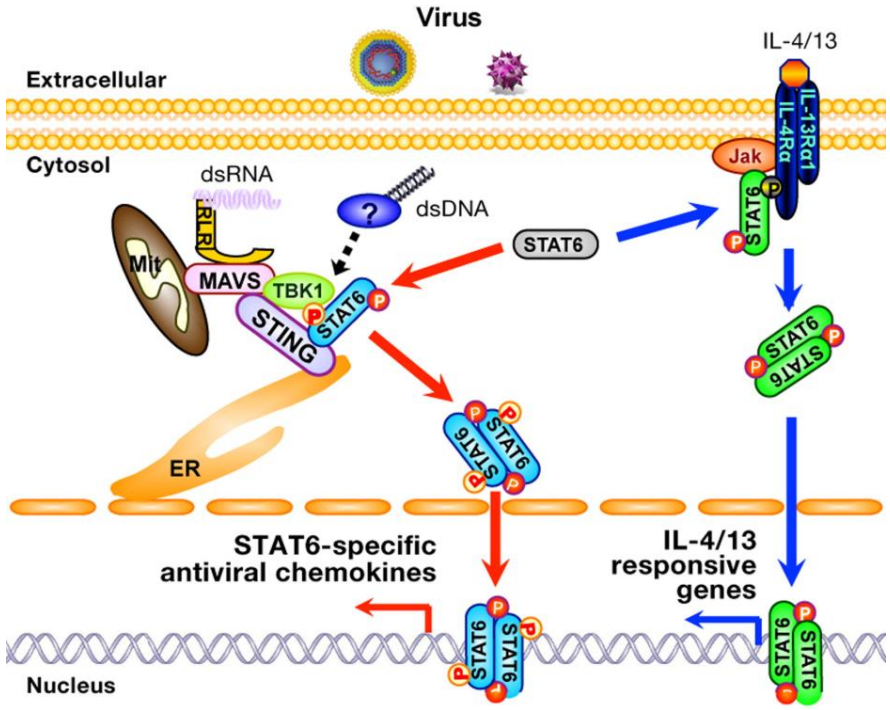
Source: Maik Friedrich et al Therapeutic siRNA: state-of-the-art and future perspectives, *BioDrug* **36**, 549–571 (2022). https://doi.org/10.1007/s40259-022-00549-3.

As siRNA agents are prone to degrade quickly, they need to be protected from their environment by a shield that is usually made of lipid nanoparticles. These nanoparticles encapsulate the siRNA molecules, safeguarding them from enzymatic degradation in the bloodstream and facilitating their efficient delivery into target cells. The use of lipid nanoparticles not only enhances the stability of siRNA but also improves cellular uptake, thereby increasing the therapeutic potential of gene silencing strategies.

STAT-6

The STAT-6 protein (Signal Transducer and Activator of Transcription 6) is a critical transcription factor primarily known for its central role in regulating the Type 2 immune response. It acts as a dual signalling molecule and gene activator, transmitting signals from the cell surface directly to the nucleus to regulate gene expression.

Simplified STAT-6 signalling pathway



Source: Huihui Chen et al, Activation of STAT6 by STING is critical for antiviral innate immunity, 2011, Cell, 147, 436-446.

STAT-6 becomes activated in response to cytokines such as interleukin-4 (IL-4) and interleukin-13 (IL-13), which are key drivers in allergic inflammation and immune modulation. Upon activation, STAT-6 dimerises and translocates to the cell nucleus, where it binds specific DNA sequences to initiate transcription of target genes involved in immune cell differentiation, survival, and function.

While JAK inhibitors are capable of preventing the phosphorylation and subsequent activation of STAT proteins, they may also affect additional signalling pathways due to their upstream mechanism of action. This broad inhibition can potentially lead to a higher incidence of adverse events, as multiple cellular processes may be disrupted. In contrast, STAT inhibitors offer a more targeted approach, acting directly on the STAT proteins themselves and thereby reducing the likelihood of off-target effects and associated toxicity.

STAT-6 plays a central role in regulating immune responses, especially those linked to allergies, asthma, and inflammation. It acts as a molecular "switch" that turns on specific genes when the immune system is stimulated.

Beyond allergy and inflammation, STAT-6 has clinical relevance in cancer biology[9]. Certain tumours, such as solitary fibrous tumours, show strong STAT-6 expression, which pathologists use as a diagnostic marker. In these cases, immunohistochemistry tests for STAT-6 help distinguish tumour types and guide treatment decisions.

Roquefort's STAT-6 siRNA therapy

Roquefort's siRNA sequences are being developed in combination with nanoparticle delivery systems to target immunology and solid cancer indications characterised by overexpression of STAT-6. Roquefort has designed multiple gene silencing constructs targeting STAT-6 mRNA.

Current status

At the time of the acquisition, the enlarged entity had expressed an interest in progressing the preclinical STAT-6 programme through IND into a Phase I clinical trial. If successful, Coiled will have two clinical assets in its pipeline.

While the company's recent focus and funding have been dominated by the proposed acquisition of the highly advanced AO-252 oncology asset, the STAT-6 programme remains an asset they intend to develop, ultimately through a Phase I clinical trial.

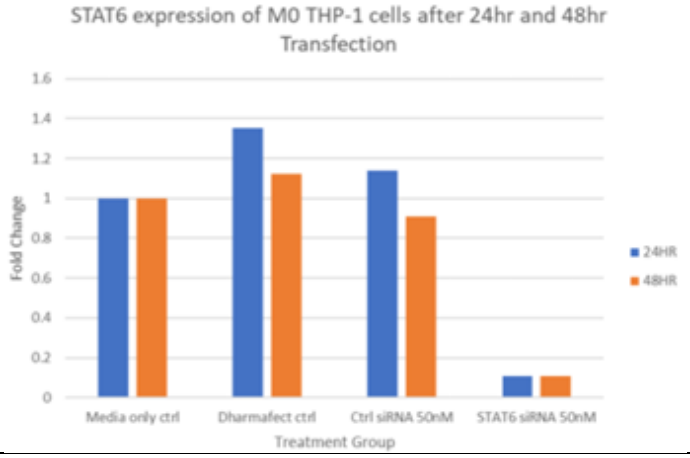
Roquefort has developed siRNAs which target the SH2 (Src-homology-2) domain of STAT6. The Company has evaluated STAT-6 targeting siRNA constructs in a cell-based model for inflammation. STAT-6 siRNA constructs were evaluated in a THP-1 macrophage cell line, which is used to evaluate treatment effects on inflammatory response. Key findings were:

- STAT-6 targeting siRNA generated a 10-fold reduction in STAT-6 expression compared to controls.
- The phosphorylated (activated) form of STAT-6 was also reduced.
- Levels of CCL17 and CD23, two key mediators in inflammatory processes, were also modified.

[9] www.mypathologyreport.ca/pathology-dictionary/stat6/

The data show how STAT-6 siRNA constructs can reduce STAT-6 gene expression and modulate inflammatory biomarkers. CCL17 is involved in allergic and Th2-type immune responses, whilst CD23 acts as a receptor that can trigger the production of inflammatory cytokines, while CCL17 is a chemokine involved in cell recruitment during inflammation.

Anti-STAT-6 siRNA generated a 10-fold reduction in STAT-6 expression



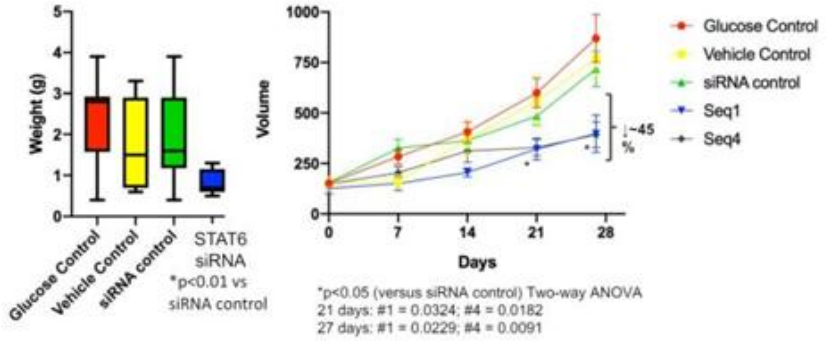
Source: Company presentation

Progress to date

Roquefort has demonstrated significant anti-cancer activity with its STAT-6 siRNA therapeutics, as validated in *in vivo* models of breast and colon cancer. These results further reinforce the potential of STAT-6 targeting approaches in multiple tumour types and provide a strong foundation for advancing this programme towards clinical evaluation.

STAT-6 targeting siRNA constructs have shown significant *in vivo* anti-cancer activity in validated models of colon cancer. STAT-6 siRNAs demonstrated a significant reduction in the proliferation of colorectal cancer with a ca.50% reduction in cell growth at seven days. This anti-cancer effect was replicated in a validated in vivo model of colorectal cancer with a significant reduction in cancer weight and volume over 28 days.

Anti-STAT-6 siRNA showed significant anti-cancer activity *in vivo*



Source: Company reports

The STAT-6 programme has made significant progress in both oncology and inflammation:

- **Pre-clinical development**: The STAT-6 siRNA therapeutics are targeting solid tumours and have shown significant *in vivo* efficacy. The programme has developed four new siRNA sequences that demonstrated efficacy in reducing

STAT-6 expression by 40-50% in validated *in vitro* models of colon cancer and tumour shrinkage in *in vivo* models.

- **Immunology and inflammation**: In September 2024, the company announced that its STAT-6 siRNA demonstrated efficacy in a validated *in vitro* experimental model of immunological disease. The experiments showed a significant reduction in the levels of STAT-6 produced compared to multiple controls at multiple time points.

Market

Our focus is on the most advanced programme with the clinical development of AO-252 in solid tumours. Due to the mechanism of action of the drug compound on the cell cycle, AO-252 could have potential in most of the solid tumours with p53 overexpression (from about 50% to 70%, depending on cancer type). Early pre-clinical data and scientific literature suggest that AO-252 may inhibit tumour cell proliferation across a broad range of solid tumour types, highlighting its promise as a versatile therapeutic candidate. Further studies are underway to define the specific tumour indications that could benefit most from AO-252, with the goal of progressing towards clinical trials in the near future.

What are solid tumours?

Solid tumours are abnormal masses of tissue that usually do not contain cysts or liquid areas. They are formed by the uncontrolled growth and division of cells. They can be benign (non-cancerous) or malignant (cancerous). The term is generally used to differentiate these types of cancers from liquid cancers or haematological malignancies like leukaemia, lymphoma, and multiple myeloma, which involve the blood, bone marrow, and lymph systems, representing only ca.10% of the whole cancer cases.

Solid tumours can arise in virtually any organ or tissue, including the breast, lung, prostate, colon, liver, and bone. They are typically classified by the type of cells they originate from:

- Carcinomas are cancers that arise from epithelial cells, which line the surfaces of organs and the body. This is the most common type of solid tumour (e.g., breast cancer, lung adenocarcinoma).
- Sarcomas are cancers that arise from connective tissues, such as bone, cartilage, fat, muscle, and blood vessels (e.g., osteosarcoma).

The key defining characteristic is their physical structure as a localised, palpable mass that often requires surgical removal and can be graded and staged based on its size, location, and whether it has spread (metastasised) to other parts of the body.

Therapeutic Approaches for Solid Tumours

The treatment plan for a solid tumour is highly customised, depending on the type, location, size, and stage of the cancer, as well as the patient's overall health. Treatment generally falls into three main categories: local treatments, systemic treatments, and supportive care.

Local Treatments

These therapies target the tumour site directly and are often the first line of defence against non-metastatic tumours:

- **Surgery:** This is often the oldest and most common treatment. The goal is to remove the entire tumour along with a margin of healthy tissue (known as a clear margin) to ensure all cancer cells are excised. Surgery can also be used for diagnosis (biopsy) or for palliative care to relieve symptoms.
- **Radiation therapy:** This uses high-energy rays (like X-rays or protons) to kill cancer cells or keep them from growing.
- **External beam radiation therapy (EBRT):** A machine outside the body aims radiation at the tumour.

- **Brachytherapy (internal radiation):** Radioactive sources are temporarily or permanently placed inside the body, directly at or near the tumour.

Systemic Treatments (Treating the whole body)

These therapies travel through the bloodstream to reach cancer cells that may have spread throughout the body (metastasis):

- **Chemotherapy:** This uses drugs (cytotoxics) to kill quickly dividing cells, including cancer cells. It is given intravenously or orally. It can be used *neoadjuvantly* (before surgery to shrink the tumour), *adjuvantly* (after surgery to kill remaining cells), or as a primary treatment for advanced disease.
- **Targeted therapy:** These drugs focus on specific molecular targets (like proteins, genes, or blood vessels) that contribute to the cancer's growth and survival. Unlike traditional chemotherapy, they are designed to limit harm to healthy cells. Examples include:
- **Tyrosine kinase inhibitors (TKIs):** Block signalling pathways essential for cancer growth.
- **Monoclonal antibodies:** Block specific receptors on the surface of cancer cells.
- **Immunotherapy (immuno-oncology):** This category of drugs harnesses the body's own immune system to recognise and destroy cancer cells.
- **Immune checkpoint inhibitors (ICIs):** Drugs like PD-1 or CTLA-4 inhibitors "release the brakes" on immune cells, allowing them to attack the tumour.
- **CAR T-cell therapy** (though primarily used for liquid tumours, research is ongoing for solid tumours).
- **Hormone therapy:** Used for cancers that are sensitive to hormones (like breast and prostate cancer). This therapy either blocks the body's production of hormones or blocks hormone receptors on the cancer cells.

Other/Combined Approaches

The vast majority of solid tumour care involves a multidisciplinary approach, combining two or more of these methods for the best outcome, depending on the stage of cancer, the type of cancer and the number of rounds of therapies needed. Decisions regarding treatment plans are typically made by a team of specialists, including oncologists, surgeons, radiologists and pathologists, to ensure that each patient receives a tailored and comprehensive strategy. This collaborative approach helps maximise treatment effectiveness while minimising side effects and complications.

Size of the solid tumour market

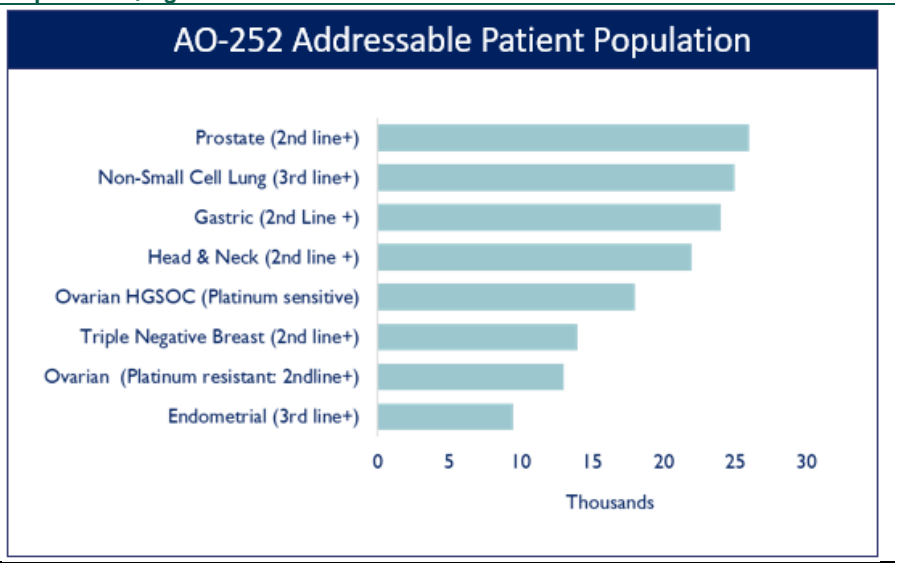
As for a novel target, to assess the addressable market TACC3 overexpression is not universal, but it is frequent and clinically significant across many solid tumours. Its presence is strongly associated with poor prognosis, metastasis, and advanced disease stage, making it a promising biomarker and therapeutic target. Meta-analyses show that a substantial proportion of patients, often 30–60% depending on tumour type, exhibit elevated TACC3 expression[10].

In the following graph, Coiled indicated an estimated addressable market of approximately 150,000 patients across the various solid tumour types in the US alone. This figure underscores the significant clinical need and commercial potential for therapies targeting TACC3 overexpression, particularly given its

[10] *June Wang et al. TACC3 as an independent prognostic marker for solid tumors: a systematic review and meta analysis, Oncotarget, 2017; 8:75516-75527. https://doi.org/10.18632/oncotarget.20466*

prevalence and association with poor outcomes in a considerable subset of solid tumour cases that possess P53 mutation and high centrosomal amplification.

AO-252 addressable market, based on TP53 mutation/high centrosomal amplification/high TACC3

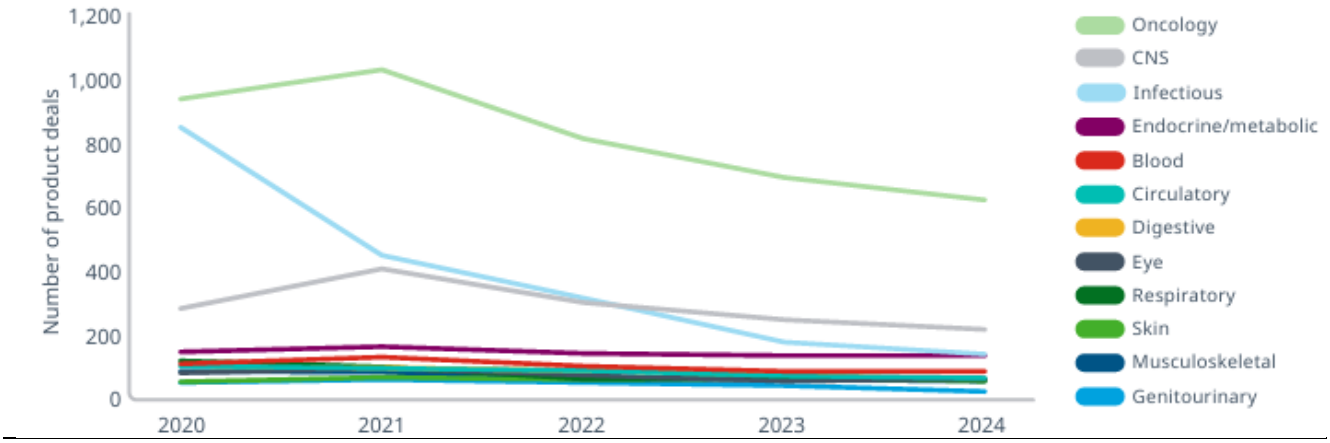


Source: Company presentation

Attractiveness of oncology assets

The figure below provides an analysis of product-related transactions, including acquisitions, licensing agreements, options to license, co-development, and collaborative research and development, by indication area. In 2024, oncology remained the leading therapeutic area for dealmaking within the life sciences sector. While the overall volume of deals decreased on an annualised basis, this trend was consistent with broader deal activity. Among deals in 2024 where an indication could be established, approximately 40% involved therapeutics, diagnostics, or medical devices targeting cancer, maintaining the same proportion as observed in 2023.

Number of product deals by therapeutic area, 2020-2024



Source: IQVIA Pharma Deals – Review of 2024

Financials

Valuation

In our view, the pharmaceutical industry consistently monitors emerging and disruptive technologies such as AO-252, indicating that this asset may be of considerable interest to major pharmaceutical and biotechnology companies. Accordingly, it is pertinent to consider the valuations and terms that leading pharmaceutical and biotech firms are willing to offer for access to molecules of this nature.

Comparative valuation - licensing deals

Coiled's strategy is to develop its assets through a Phase I clinical trial, then to license them to a suitable partner. The following table provides some indication of the value that big pharma and biotechs are willing to pay to access a small molecule Phase I clinical asset in the field of oncology.

This list is not comprehensive; it examines only transactions with publicly disclosed financial details. Numerous other deals exist where such information has not been made available. Our primary interest has been in transactions involving assets that are either in Phase I or ready to enter Phase I.

Date	licensor	licensee	Asset Type / Target	Clinical status	Upfront payment (app.)	Total deal value (incl. milestones)
Jul-21	Lilly	Kumquat Biosciences	Small Molecule Platform (Undisclosed Targets)	Discovery/Preclinical	$70m	Up to $2,000m
Sep-22	Merck KGaA	Nerviano Medical Sciences	PAPR1 inhibitor	Phase I	$65m	Undisclosed
Mar-23	Amgen	Volastra	KIF18A Inhibitor (Sovilnesib/AMG 650)	Phase I	$60m (Series A funding)	-
Dec-23	Merck	C4 Therapeutics	Degrader-Antibody Conjugates (DACs) (Small Molecule Focus)	Preclinical/IND	$10m	Up to $600m
Dec-23	GSK	Hanosh Pharmaceuticals	B7-H3 ADC (ADC has small molecule payload)	Phase I/II	$185m	Up to $1,525m
Jan-24	GSK	IDRX	KIT TKI (Tyrosine Kinase Inhibitor) for GIST	Phase I/II	Acquisition	Up to $1,150m
Mar-24	Merck	C4 Therapeutics	Targeted Protein Degraders (MGDs)	Preclinical/IND	$16m	Up to $740m
Apr-24	Novartis	Arvinas	ARV-766 PROTAC androgen receptor degrader	Phase I	$150m	Up to $1,010m
Oct-24	Pfizer	Triana Biomedicines	Molecular Glue Degraders (MGDs)	Preclinical/IND	$49m	Over $1,500m
Oct-24	Novartis	Monte Rosa Therapeutics.	Molecular Glue Degrader (MRT-6160)	Phase I	$150m	Up to $2,300m
Feb-25	AbbVie	Xilio Therapeutics	Tumour-activated Immunotherapy (Small molecule/Antibody combo)	Phase I	$52m	Up to $2,100m
Mar-25	Servier	Black Diamond Therapeutics	BDTX-4933 (RAS/RAF-mutant Inhibitor)	Phase I	$70m	Up to $710m
May-25	Genentech	Orionis Biosciences	Small Molecule MGDs (Molecular Glue Degraders)	Preclinical/IND-enabling	$105m	Over $2,000m
Jun-25	Gilead	Kymera Therapeutics	CDK2 Molecular Glue Degrader	Phase I (IND-enabling)	$85m	Up to $750m
Jun-25	BMS/RayzeBio	Philochem	Radiopharmaceutical Small Molecule (OncoACP3)	Phase I	$350m	Up to $1,400m
Jul-25	Debiopharm	Repare Therapeutics	PKMYT1 Inhibitor (Lunresertib)	Phase I	$10m	Up to $267m
Nov-25*	J&J	Halda Therapeutics	HD-0915 protein-protein "glue"	Phase I/II	Acquisition	$3,050m
Nov-25	Gilead	Sprint Bioscience	TREX1 programme	Preclinical	$14	$400m
				Average	**$85m**	**$1,344m**
				Median	**$67m**	**$1,275m**

Source: SP Angel

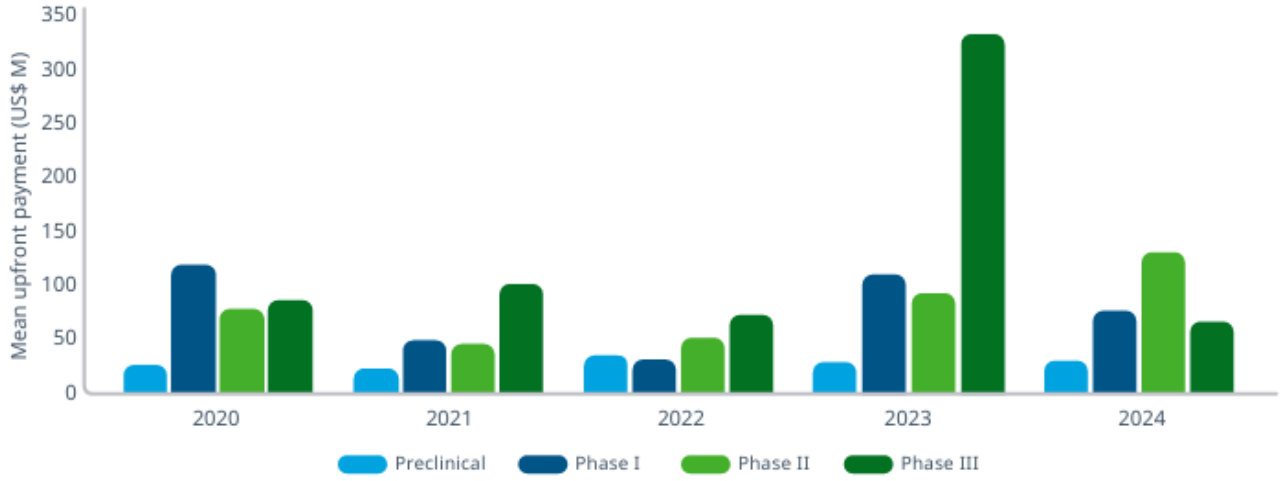
*See the following paragraph

The median up-front licence deal value of preclinical compounds in the Phase I space is $67m (ca.£51m), with milestones of up to $1,275m (ca.£957m). There is a big discrepancy between deals due to a number of factors, such as:

- the number of programmes within the deal;
- the size of the market;
- the type of target; and
- the potential market.

Moreover, the figure below from IQVIA presents upfront cash payments for each phase of the drug development (for all therapy areas) from 2020 to 2024. The mean upfront cash payment does not differ much between the different phases from preclinical to Phase III (the 2023 Phase III median upfront of ca.$350m takes into account the $5.5bn upfront in the Daiichi/Merck deal.

Mean upfront payment for licensing deals by development stage, 2020-2024



Source: IQVIA Pharma Deals – Review of 2024

Phase I programmes continued to command high upfront values in 2024, with the mean upfront payment for deals at this development stage reaching ca.$75m (£57m) (or $67m/£51m from our previous table), mainly due to the Merck-LaNova and Arrowhead-Sarepta deals, both with upfront payments exceeding $500m.

Roquefort's acquisition of the AO-252 license, with an upfront consideration of £31.875m, closely aligns with the mean value of £57m. An additional factor to consider is the innovative nature of the target asset. AO-252 is characterised as a novel, first-in-class, first-in-human therapeutic agent directed at the TACC3 protein. Given its novelty, the associated risk is greater and therefore discounted when compared to that of less risky assets but could possibly hold a much greater potential due to the novelty.

Sector highlight: $3bn Halda Therapeutics acquisition by J&J

In November 2025, J&J acquired Halda Therapeutics for £3.05bn to get access to its innovative RIPTAC™ platform (Regulated Induced Proximity Targeting Chimeras). Halda Therapeutics is developing a drug platform for a new class of cancer treatments called RIPTAC™ therapeutics. These are heterobifunctional protein-protein interaction inhibitor drugs designed to selectively induce cell death in cancer cells by pairing specific ligands and linkers, through a "hold and kill"

mechanism. The company has built a discovery engine that takes these therapies from conception through design, optimisation, and preclinical/clinical testing.

Both Halda's RIPTAC™ platform and Coiled's AO-252 are built on the principle of exploiting cancer-specific vulnerabilities through protein–protein interactions, aiming to selectively kill tumour cells while sparing normal tissue.

RIPTAC platform

Source: Halda Therapeutics

The lead molecule, HLD-0915, is an oral, once daily RIPTAC therapeutic currently in Phase I/II clinical development for metastatic castration-resistant prostate cancer (mCRPC). HLD-0915 is designed to selectively target prostate cancer tumours cells by holding together, with defined orientation and purpose, androgen receptor (a tumour-specific intracellular targeting protein) and BRD4, an oncogenic protein and a major driver in many cancers. The ternary complex drives the formation of new protein-protein interactions, abrogating BRD4 function selectively within cancer cells which results in an anti-tumour effect.

Early first-in-human results have shown encouraging safety, and the findings demonstrate that HLD-0915 was well-tolerated and showed encouraging preliminary signs of anti-tumour activity, including reductions in prostate-specific antigen (PSA) and circulating tumour DNA (ctDNA), and responses by RECIST, in patients with advanced mCRPC who had progressed on up to eight prior therapies. Anti-tumour activity was observed at all doses and occurred in patients with heterogeneous, adverse molecular characteristics.

It is probably the remarkable anticancer activities on advanced prostate cancer patients together with a strong early safety profile that triggered J&J's decision to pay the hefty $3.05bn to acquire Halda and its proprietary platform, as the announcement came shortly after the company disclosed early results of its Phase I/II in mCRPC with HLD-0915.

Company matters

Registration

Roquefort Therapeutics plc was incorporated on 17 August 2020 in England and Wales with company number 12819145 under the Companies Act.

The address of its registered office is:

85 Great Portland Street
First Floor
London W1W 7LT

Tel: +44 (0)20 3918 8633
The Company's main country of operation is the United Kingdom.

Board of Directors (post readmission)

Position	Name	Remuneration	Audit
Executive Chairman	Dr Sotirios Stergiopoulos		
Chief Executive Officer	Sridhar Vempati		
Non-Executive Director	Stephen West	Member	Chair
Non-Executive Director	Jean Duvall	Member	Member
Non-Executive Director	Pamela Frank	Chair	Member

Dr Sotirios Stergiopoulos – Executive Chairman

Dr Stergiopoulos is a physician executive with significant experience in the Pharmaceutical/Biotech industry, especially in Oncology. He is the former Chief Medical Officer of multi-billion dollar Euronext-listed Ipsen and has held appointments as an Attending Physician and trainee in institutions such as Albert Einstein College of Medicine, Harvard Medical School and the National Institutes of Health. He holds a Master's in Biotechnology, Enterprise and Entrepreneurship (MBEE) from The Johns Hopkins University and a Medical Degree from Poznan University of Medical Sciences (Poland). Sotirios is a Fellow of the American College of Physicians, the New York Academy of Medicine, as well as the Royal Society of Medicine (UK). He is also a Member of the American Association for Cancer Research and of the American Society of Clinical Oncology. In October 2017, Dr Stergiopoulos was appointed President of the Board of Governors for the Accreditation Council for Medical Affairs (ACMA).

Sridhar Vempati – Chief Executive Officer

Mr Vempati brings nearly two decades of extensive expertise in drug discovery, oncology research, and business strategy with a track record of advancing novel therapeutics from concept to clinical development. Prior to founding Coiled Therapeutics, he co-founded A2A Pharma in 2016, where he serves as Chief Strategy Officer and Executive Vice President of Research and Development, overseeing computational drug design platforms and pipeline advancement. Earlier in his career, he held forecasting and business development roles at Ironwood Pharmaceuticals and Rafael Pharmaceuticals and served as an Equity Research analyst at Jefferies LLC, analysing biotechnology investments. He has completed a postdoctoral fellowship in leukaemia research at Dana Farber Cancer Institute (Harvard University). He holds a PhD in molecular biology from Ludwig-

Maximilians-University, Germany, an MBA from Boston University, and an MS degree from Guru Nanak Dev University, India.

Stephen West – Non-Executive Director

Mr West is an experienced Fellow Chartered Accountant (CA ANZ) and ACA (ICAEW), with over 30 years' financial and corporate experience gained in public practice, life sciences, oil and gas, mining and investment banking. Mr West has held several senior positions in public companies. These included PetroNor E&P Limited, where he was Executive Director and Chief Financial Officer and instrumental in the successful $100m merger of African Petroleum Corporation Ltd and PetroNor E&P Limited in August 2019. Mr West was also a Non-Executive Director of ASX-listed Apollo Consolidated Limited, a company acquired for A$181m in 2021. He is co-founder and non-executive director of TollCyto Therapeutics Ltd and Paris Bio Ltd. Mr West is currently Executive Chairman of Roquefort Therapeutics and will transition to Non-Executive Director upon completion of the acquisition.

Pamela Frank – Non-Executive Director

Ms Frank is an accomplished executive leader with over 30 years of experience in strategic coalition building, regulatory advocacy, and governance across complex, multi-stakeholder environments. As Senior Vice President at Gabel Associates and CEO of ChargEVC, a non-profit uniting industry, government, and advocacy groups, she has successfully driven policy development, legislative outcomes, and transparent allocation of public funds, including federal infrastructure investments. Her advisory roles on New Jersey's Governor's Council on the Green Economy, Energy and Transportation Transition Teams, and the Restart and Recovery Advisory Council demonstrate deep expertise in cross-sector collaboration, risk management, and ethical oversight. A proven navigator of regulatory frameworks and public-private partnerships, Ms Frank excels in fostering accountability, aligning diverse interests, and guiding organisations through transformative change. Ms Frank holds a Master of Public Health (MPH) from the University of Medicine & Dentistry - School of Public Health and earned a Bachelor of Arts in Philosophy from the University of Vermont.

Jean Marie Duvall – Non-Executive Director

Ms Duvall is highly accomplished in the biotech and pharma sector, with over 25 years' experience in executive roles in the industry. During this time, Jean acted for Ferring Pharmaceuticals, as one of the Executive Board Members who built the company from a US$700 million to US$2 billion in revenue. Jean has a significant track record in corporate development, having led multiple successful M&A, divestment and licensing deals throughout her career. She previously had the role of General Counsel at Elan Corporation and was legal lead, negotiating the divestment of over $2 billion in assets. Additionally, she has co-founded and led biopharma start-ups, including Trizell and Amzell, resulting in multiple products having successful phase 2 and 3 clinical studies. Jean is currently CEO and co-founder of ReproNovo SA and a non-executive director of Ondine Biomedical Inc. (AIM:OBI).

Risk

Investments in small, early-stage pharmaceutical companies carry a significant risk, and investors must be aware of this fact. In our opinion, the following risks are particularly relevant. Each of them could have an impact on time to reach market, cashflow-breakeven and profitability.

Dilution risk

The company has sufficient cash to fund the ongoing clinical trial and preparation for the IND for the STAT6 programme but may need more capital to undertake further projects. There is no guarantee that the company will be successful in raising such funds, nor on the terms that such capital is raised, which could be dilutive to existing shareholders.

Early-stage development

Coiled focuses on advancing programmes that are still at an early stage, which exposes the company to significant risks related to research and development, regulatory approval, and drug safety.

Commercialisation

The strategy of management is to develop clinical assets for commercialisation to suitable partners and to receive an up-front on signature, milestones and royalties. The time taken to reach such agreements can be long, and there is no guarantee that this would be on terms that are beneficial to shareholders. However, there is a willingness of big pharma and biotech to acquire novel assets, especially when there are interesting new targets. The greater the level of data and type of targets, and hence de-risking, the more that commercial partners are willing to pay.

Patent robustness

As with all IP-rich companies, there is a risk that the intellectual property is insufficiently covered by global patents, allowing a competitor to gain market access. Any litigation could involve high costs and uncertainties.

Share liquidity

As with many small-cap companies listed on AIM, there can be difficulty in buying and selling shares in volume. Market makers only guarantee prices in a very small number of shares.

Competition

The Company operates in a competitive field that attracts much R&D investment, often dominated by large multinational players, most of which have significant financial resources to fund development programmes, marketing activities, etc.

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