SP Angel Healthcare

Roquefort Therapeutics (ROQ.L)

5 September 2024

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ROQUEFORT THERAPEUTICS PLC

Source: Roquefort Therapeutics

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Healthcare Research

Non-Independent Research
MiFID II Exempt

5 September 2024

*SP Angel acts as Broker to Roquefort Therapeutics

Stock Data

Ticker	ROQ.L
Share Price:	3.6p
Market Cap:	£4.6m

Source: London Stock Exchange (prior trading day's close)

Company Description

Preclinical stage developer of novel therapeutics for difficult to treat cancers

Share price (p)

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Roquefort Therapeutics (ROQ.L*)

Developing a diverse pipeline of medicines focused on immunology and oncology

Key points

- **Focus on novel targets in oncology and immunology:** Including STAT-6, Midkine and Natural Killer (NK) cells. There are currently no approved therapies which directly target STAT-6 or Midkine.
- **Preclinical proof of concept data across the pipeline:** Roquefort has generated *in vivo* or *in vitro* efficacy and safety data on its portfolio with activity across a number of diseases.
- **Mesodermal Killer (MK) cells represent new class of cell therapy** and a promising form of immunotherapy which can act as an adjuvant for NK cells in an oncology and immunology setting. We believe this programme to be a signficant driver of future value to the business.
- **STAT-6 siRNA asset positioned in a high interest area** highlighted by a Sanofi (SAN.EPA)/Recludix (Private) deal for a preclinical STAT-6 inhibitor with a US$125m upfront payment and up to $1.2bn in conditional milestones.
- **Proven track record to strike deals at the preclinical stage** demonstrated by agreements with Randox Laboratories (Private) and PDC-CRO (Private), subject to final terms.
- **PDC-CRO deal could generate up to US$10m initial consideration** including $1.3–$2.5m in cash as well as a c.25% stake in any proceeds if the assets are subsequently sold.
- **Strong IP estate** with patents across the five programmes including significant protection for Midkine-targeting therapies.

Roquefort Therapeutics ("Roquefort", "the Group", "the Company") is a preclinical-stage biotechnology business developing a differentiated pipeline of medicines which include small interfering RNA (siRNA), Midkine-targeting molecules and a novel form of cell therapy, termed MK cells. MK cells have been shown to recruit and activate Natural Killer (NK) cells. MK Cells also have potential applications in the immunology space. Cell therapy remains an area of industry interest with a number of deals struck at a preclinical stage.

Roquefort aims to create shareholder value by generating preclinical proof of concept data across its pipeline with a view of striking licencing agreements to support clinical development and commercialisation activities. Management has a proven track record in licensing biotech assets and recently signed a term sheet to license its Midkine antibody programme to PDC-CRO, a leading clinical research organisation. Subject to signing of a definitive licence agreement, Roquefort expects to be eligible for $10m initial consideration, which is expected to include a $1.25m – $2.50m cash component, as well as the share of any future trade sale proceeds if the assets are sold. On the back of positive Phase 1 data, this could generate up to $50m to the Group, based on comparable sales which took place at a similar stage. There continues to be considerable corporate activity in oncology with multiple deals focused on assets at Phase 1 or preclinical stage, highlighting the significant opportunity across the company's portfolio. With a diverse, early-stage pipeline and a proven record of striking commercial deals, we believe Roquefort remains undervalued compared to its peers at a similar stage operating in the oncology space.

Investment Thesis

Roquefort is looking to maximise shareholder value by developing its assets to key milestones, such as preclinical proof of concept or early clinical trials, and then striking out-licensing deals. Industry data showed that the median upfront component for deals struck at Phase 1 is c.$100m (Source: Dealforma 2023 Annual Biopharma Report).

Leader in Midkine therapeutic development

Following the acquisition of Lyramid, Roquefort has become a leader in the development of medicines which target Midkine. Midkine is a human growth factor associated with several diseases and represents a novel therapeutic target. Elevated levels of Midkine have been associated with poor prognosis, increased tumour size, and a higher likelihood of metastasis. There are no drugs available which target Midkine. Roquefort benefits from over 10 years of preclinical research by Lyramid which has demonstrated the therapeutic potential of Midkine-based therapies in several disease areas. Development is supported by a portfolio of 37 patents in the Midkine space.

PDC-CRO deal could generate $10m upfront consideration

Roquefort recently signed a term sheet to out-license its Midkine antibody portfolio to PDC-CRO, a leading clinical research organisation based in the Middle East and Africa region. The proposed agreement, pending the signing of a definitive license agreement, will place the Midkine antibody assets into a special purpose vehicle (SPV). Roquefort will be eligible for an initial consideration of $10m, including non-dilutive equity in the SPV, and expects an upfront payment of $1.3 – 2.5m. Additionally, Roquefort expects to receive a 24% share of any future trade sale proceeds of the SPV. If a Phase 1 trial is successful, management estimates that their 24% stake in the SPV could be worth up to $50m. This is corroborated by recent data showing the median upfront component for deals struck at Phase 1 stage is c.$100m (Source: Dealforma). This excludes conditional milestone or royalty payments that can bring the total deal value above $1bn. The PDC-CRO deal shows the ability of the management team to strike commercial agreements.

Diversified asset pipeline with encouraging preclinical data

Roquefort is developing assets across a number of treatment modalities. Alongside its Midkine-antibody programme, the Group is also developing various nucleic acid-based treatments that modulate the expression levels of Midkine and STAT6, a transcription factor implicated in cancer progression. The development of the STAT6 siRNA programme highlights the Group's internal R&D capacity to develop new treatment candidates, complementing management's ability to select and acquire external programs. This diversified platform reduces reliance on any single asset and provides a wide range of opportunities to generate value and look to strike licencing agreements.

MK cell therapy has applications in oncology and immunology

Alongside the nucleic acid and antibody-based assets, Roquefort is progressing development of Mesodermal Killer (MK) cells which recruit and activate natural killer (NK) cells, MK cells represent a proprietary form of cell therapy. MK cells target diseased cells both directly and by enhancing the activity of NK cells. Given the high industry interest in NK cells, we expect this asset to generate significant interest should the group

produce early clinical stage data. This has been highlighted by the $167m IPO of Artiva Biotherapeutics (ARTV.NQ) which completed in July 2024.

Focus on high value diseases with limited treatment options

Roquefort is evaluating its treatments in a number of disease indications with a high unmet need. This includes immunology indications and cancer types including advanced lung and breast cancers, blood malignancies and rare diseases, such as osteosarcoma, a form of bone cancer. Osteosarcoma provides an opportunity to showcase the potential of the Midkine-targeting treatments for an underserved cancer indication. Given the demand for effective osteosarcoma treatments, there is also precedent for Roqueforts assets to qualify for expedited approval programmes, such as FDA Breakthrough Therapy designation and orphan drug designation. This could result in the Group receiving tax credits for clinical trial costs, waived regulatory fees, and eligibility for marketing exclusivity. This could significantly reduce the time and costs associated with developing Roquefort's assets and make these programmes more attractive to potential buyers.

Management team has strong track record of licensing assets

Roquefort has assembled a skilled team to provide comprehensive support across all aspects of the business. This includes significant expertise in running life-science companies both in large multinationals and smaller biotechnology companies as well as experience in academia, R&D and marketing. Ajan Reginald, CEO, has a proven track record of striking licensing agreements. At Roche (ROG.SW) he was involved in a number of in-licencing transactions for a number of assets. At Celixir (Private) he struck an agreement with Daiichi Sankyo (4568.TY), a major Japanese multinational pharma company. This deal included a £12.5m upfront payment for the Japan market alone and an £5.0m equity investment at a £200m valuation. The team is supported by non-executive directors with considerable expertise in the field of academia and drug development. This includes Professor Sir Martin Evans who won the Nobel Prize for Medicine in 2007 for his research on stem cells and Dr Darren Disley who co-founded Horizon Discovery, which was sold to PerkinElmer in 2020 for £300m.

Development protected by strong IP

Roquefort is developing an IP estate which provides adequate patent protection for its products and platform in all key jurisdictions. Roquefort has the exclusive worldwide licence to commercialise MK cells, STAT6 siRNA and Midkine-based therapies.

Upcoming Newsflow

The Company has several future milestones which it looks to achieve across the short and medium term. In the short term, we expect the Group to finalise the PDC-CRO agreement regarding the Midkine-antibody programme. Longer term we anticipate the Group to strike additional partnerships across its pipeline.

We also expect Roquefort to progress preclinical development of its asset pipeline. This includes generating *in vivo* data on its MK cell therapy and progressing preclinical work on the STAT6 and Midkine-focused siRNA/mRNA programmes.

Peer-group review

Roquefort is trading well below its peers

We have collated a peer group of preclinical or early clinical-stage drug developers (Table 1). We have included businesses that are listed in London as well as global peers that are developing treatments in the cell therapy or gene silencing space.

In terms of its peers, the median market capitalisation (£70.3m) and enterprise value (£29.9m) remains significantly higher than that of Roquefort Therapeutics (Market capitalisation £4.6m; Enterprise value £4.1m).

Given that Roquefort has a platform-based offering which can deliver multiple assets, across a wide range of indications, as well as commercial deals in place for its Midkine antibody platform, we believe the business has considerable upside potential.

Table 1: Peer Group Review

Name	Ticker	Mkt Cap (£m)	Enterprise Value (£m)	Lead asset stage	Lead Candidate (s)	Lead indication (s)	Lead Candidate type (s)
Average		**142.7**	**102.3**				
Median		**70.3**	**29.9**				
Roquefort Therapeutics	**ROQ LN**	**4.6**	**4.1**	Preclinical	STAT-6 siRNA, MK cells, anti MDK Ab	Immune/oncology	siRNA, ASO, Cell therapy, antibodies
Artiva Biotherapeutics	ARTV US	203.8	338.0	Phase 1	AlloNK	Lupus nephritis	NK cell therapy
Acepodia Inc	6976 TT	342.4	195.7	Phase 1	ACE1831	CD20+ NHL	Anti CD20 γδ2 T-cell therapy
Avacta Group	AVCT LN	262.6	269.3	Phase 1	AVA6000	Solid tumours	Affimer-based targeted treatment
Chimeric Therapeutics	CHM AU	7.3	5.4	Phase 1	CHM 0201	AML	NK cell therapy
Fate Therapeutics	FATE US	299.4	143.6	Phase 1	FT576/FT819	r/r MM; r/r ALL & DLBCL	BCMA, CD38/CD19 CAR-T cell therapy
Kyverna Therapeutics	KYTX US	241.8	-24.1	Phase 1	KYV-101	Multiple Sclerosis	anti-CD19 CAR T cell therapy
Nkarta	NKTX US	276.9	87.7	Phase 1	NKX101	AML	anti-NKG2D cell therapy
Nkgen Biotech	NKGN US	15.2	28.4	Phase 1	SNK01	Parkinson's Disease	NK cell therapy
Tscan Therapeutics	TCRX US	217.6	54.2	Phase 1	TSC-100	Bone marrow transplants	T cell receptor (TCR)- therapies
Turnstone Biologics	TSBX US	12.0	-35.6	Phase 1	TIDAL-01	Breast/colorectal cancer	Tumour infiltrating lymphocyte
Vigencell	308080 KS	45.5	21.5	Phase 1	VT-Tri(1)-A	r/r AML	Antii WT1, Survivin, and TERT NK cell
Celyad Oncology	CYAD BB	8.4	3.2	Phase 1 b	NKG2D	r/r AML	NKG2D-based CAR T-cell therapy
Celularity	CELU US	47.9	83.4	Phase 1/2	CYNK-001	r/r AML and r/r MM	NKG2D and CD94 NK Therapy
Faron Pharmaceuticals	FARN LN	231.2	216.6	Phase 1/2	Bexmarilimab	Solid tumours	anti-CLEVER-1 antibody
Sangamo Therapeutics	SGMO US	128.4	129.4	Phase 1/2	TX200	Fabry disease	anti-HLA CAR-T cell therapy
Sareum Holdings	SAR LN	31.8	31.4	Phase 1/2	SDC-1801	Psoriasis	TYK2/JAK1 inhibitor
Scancell Holdings	SCLP LN	153.4	160.1	Phase 1/2	Modi-1	Solid tumours	Cancer vaccine
Arecor Therapeutics	AREC LN	30.2	23.9	Phase 2	AT247	Diabetes	Ultra-Rapid Acting Insulin
Theracryf	TCF LN	3.0	1.0	Phase 2	SFX-001	Breast Cancer	Small molecule
Inmune Bio	INMB US	92.7	72.4	Phase 1	INKmune	AML/ Prostate cancer	TIML-NK cell therapy
Cytomed Therapeutics	GDTC US	13.1	8.0	Preclinical	CTM-N2D	r/r solid tumours	iPSC-derived NK cell therapies
Senti Biosciences	SNTI US	9.2	24.9	Preclinical	SENTI-202	r/r AML	anti CD33/FLT3 CAR-NK cell therapy
Cero Therapeutics	CERO US	4.5	10.8	Pre-clinical	CER-1236	r/r AML, MCL, CLL	CER-T cell therapy
Portage Biotech Inc	PRTG US	3.0	-1.5	Phase1/ 2	PORT-2	Non-small cell lung cancer	small molecule NK T cell engagers
Century Therapeutics	IPSC US	105.9	-4.9	Phase 1	iNK	B-cell malignancies	iPSC-derived NK cell therapies
Bivictrix Therapeutics	BVX LN	6.2	4.6	Preclinical	BVX001	AML	ADC
4basebio Plc	4BB LN	185.8	192.2	Preclinical	undisclosed	Duchenne muscular dystrophy	gene therapy restoring function of dystrophin gene
Hemogenyx Pharma	HEMO LN	17.6	19.3	Preclinical	HEMO-CAR-T	AML	anti-FLT3 CAR-T
Silence Therapeutics	SLN US	680.4	626.6	Phase 2	Zerlasiran	Cardiovascular disease	anti LPA siRNA
Stoke Therapeutics Inc	STOK US	603.0	382.8	Phase 1	STK-001	CNS/ophthalmology	antisense oligonucleotides (ASOs)

Source: Bloomberg; Company announcements; Natural Killer (NK); Acute Myeloid Leukaemia (AML); Relapsed/Refractory (r/r); Multiple Myeloma (MM) Acute Lymphoblastic Leukaemia (ALL); Mantle Cell Lymphoma (MCL); Chronic Lymphocytic Leukaemia (CLL); Central Nervous System (CNS); Diffuse Large B-Cell Lymphoma (DLBCL)

Company overview

Roquefort company history

Listed on LSE with a focus on acquiring preclinical assets

Listed on the Standard list segment of the London Stock Exchange in 2021 and acquired Midkine specialist Lyramid in 2021 and Oncogeni in 2022

Roquefort Therapeutics is a UK-based, preclinical stage, biotechnology company focused on the development of immune / oncology medicines. The Company, founded in 2020, is headquartered in London, UK with laboratory facilities in Stratford-upon-Avon. Initially called Roquefort Investments, the business was formed to pursue opportunities in the biotechnology sector. In March 2021, the Company listed on the Standard List segment of the London Stock Exchange.

Acquisition of Lyramid created a leader in Midkine therapeutics

In December 2021, Roquefort completed the acquisition of Lyramid Pty Limited, an Australian preclinical-stage biotechnology business. Lyramid was acquired for an initial consideration of £1m, split equally between cash and shares. The transaction constituted a reverse takeover with Roquefort Investments changing its name to Roquefort Therapeutics.

Pipeline consists of five preclinical stage assets spanning antibodies, oligonucleotides and cell and gene therapies

Lyramid was formed in 2016 to commercialise IP surrounding Midkine, a novel cancer target. The group has the exclusive worldwide licence to commercialise up to 37 patents related to the use of Midkine-based therapies for the treatment of severe inflammatory diseases, autoimmune disorders and cancer. The acquisition of Lyramid brings over 10 years of research and c.AU$40m of investment into Midkine R&D. Alongside the acquisition, Roquefort completed a £3m fundraise to fund the acquisition and support preclinical drug development activities.

Acquisition of Oncogeni brought in novel RNA and cell therapy platforms

In September 2022, Roquefort acquired the entire issued capital Oncogeni for a consideration of £5.5m, satisfied by the issue of shares. Oncogeni is a preclinical stage UK-based biotechnology business which was spun-out from Celixir (Private) in 2019. The acquisition brought Roquefort two high-value programmes outside of Midkine: a novel cell therapy (MK cells) and a gene silencing programme (STAT6 siRNA). These programmes are protected by nine patents. Alongside the acquisition, Roquefort raised £1.0m.

Product pipeline summary

Roquefort benefits from a diversified portfolio spanning several drug modalities. This includes antibodies and nucleic acid (oligonucleotides and mRNA) which target Midkine as well as a gene silencing (siRNA) platform targeting STAT-6, a protein overexpressed in a number of cancers, and a novel cell therapy (MK cell) with immune / oncology applications.

Figure 1: Roquefort product pipeline

Source: Company presentation

Collaborations with medical institutions supporting R&D activities

Roquefort has several ongoing research collaborations with leading medical research institutions based in Australia. These investigator-led studies not only highlight the interest in the Group's platform but generate additional data regarding the Company's programmes. This can be used to guide the further development of these therapeutics in additional disease indications.

Table 2: Pre-clinical Collaborations

Programme (s)	Institution (s)	Activities
Midkine antibody	Olivia Newton-John Cancer Research Institute, La Trobe University, Melbourne	Breast cancer metastasis antibody programs: *in vivo* safety was successfully demonstrated in January 2023.
Midkine RNA oligonucleotide STAT-6 siRNA	Lowy Cancer Research Centre, University of New South Wales, Sydney	Liver and Colorectal cancer Midkine RNA and STAT-6 siRNA programs *in vitro* study confirmed in June 2023 that the Company's Midkine RNA oligonucleotides produced a novel non-functional Midkine protein that has been shown to produce >90% in vitro efficacy (at the mRNA level) in human liver cancer and neuroblastoma cancer cells.
Midkine antibody	Hawkins Laboratory Biochemistry and Genetics, La Trobe University, Melbourne	Lung cancer metastasis antibody programs *in vivo* safety was successfully demonstrated in January 2023, and *in vivo* efficacy results were released in June 2023 which showed a statistically significant reduction in lung metastasis, and a reduced proliferation (growth rate) of the primary tumour. The efficacy study was carried out in a validated experimental model of osteosarcoma.
Midkine RNA oligonucleotide	School of Medical Sciences, University of Sydney	Company's Midkine RNA oligonucleotides demonstrated *in vitro* efficacy in hepatocellular carcinoma liver cancer cells producing a significant reduction in full length Midkine and generated a novel non-functional Midkine.

Source: Company Prospectus

Laboratory & GMP Manufacturing Facilities

Roquefort benefited from a UK laboratory located in Stratford-upon-Avon, which was acquired as part of the Oncogeni acquisition. The facility encompasses over 5,000 sq. ft of co-located laboratory and office space. The facility includes state-of-the art clean rooms and on-site quality control laboratory. In addition, Roquefort has access to a Good Manufacturing Practice (GMP) manufacturing facility designed for the production of clinical grade medicines which previously manufactured products for US, EU and UK approved clinical trials. The availability of these facilities enables Roquefort to perform developmental and manufacturing activities on its product candidates and should generate cost savings compared to outsourcing these activities to third parties. These facilities are of particular interest for the MK cell therapy programme as the site was previously used to manufacture cell-based therapies for clinical trials.

Business model: Demonstrate proof of concept and licence to pharma

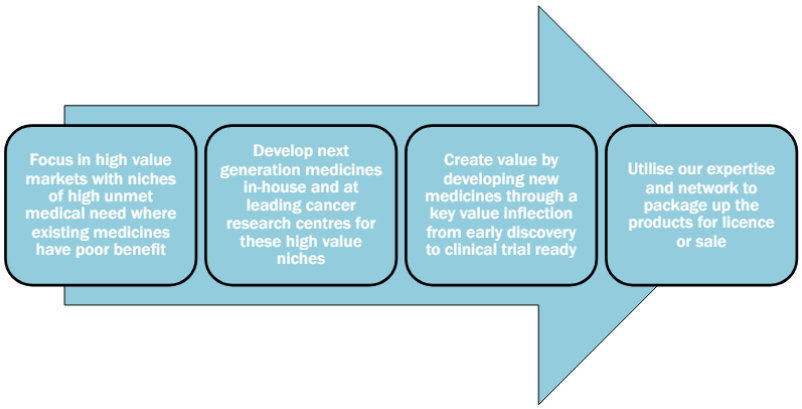
Roquefort has now integrated both Oncogeni and Lyramid and continues to make considerable progress across its pipeline. The Group aims to maximise the value of its assets through licensing deals or the sale of clinical programmes. To achieve this, management are focused on demonstrating efficacy in preclinical testing. Preclinical activities are supported by collaborations with leading medical research institutions.

Focus on generating early proof of concept and licensing to pharma for higher-risk, capital-intensive clinical, regulatory and commercial activities

The Company looks to progress its programmes towards the clinical stage by completing preclinical proof-of-concept studies which form part of the regulatory applications (IND/CTA) to request approval to conduct clinical trials. These applications contain information regarding animal pharmacology and toxicology studies, manufacturing information and clinical protocols. Alongside supporting regulatory applications, we expect this data to support potential partnership discussions. This approach has been validated by the recent PDC-CRO agreement which was struck after Roquefort had generated *in vivo* proof-of-concept data on the Midkine-antibody platform.

The Group aims to strike a balance between forming partnerships for some of the preclinical stage assets while retaining the most valuable assets to take into clinic trials. Human data is significantly more valuable than preclinical data but reaching this stage takes time and comes with additional cost and risk.

Figure 2: Roquefort business model



Source: Company presentation

Midkine overview

Midkine is a protein discovered by Professors Takashi Muramatsu and Kenji Kadomatsu at Nagoya University, Japan in 1988. Midkine is classed as a heparin-binding growth factor. These growth factors play various roles in cellular processes such as cell proliferation, differentiation, migration, and survival.

High level of Midkine expression observed in several diseases

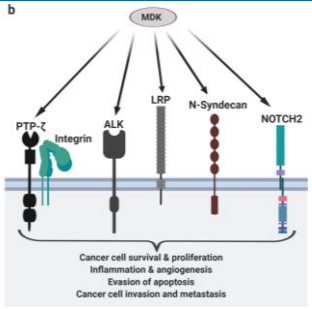
Midkine is implicated in a number of diseases…

Midkine has a significant role in embryonic development but is subsequently expressed at modest levels in healthy tissues. However, research has demonstrated that Midkine is significantly upregulated in several inflammatory diseases and various forms of cancer. This profile of high expression in diseases cells and low expression in healthy cells makes Midkine a promising therapeutic target as well as a diagnostic biomarker.

…and is responsible for driving cancer cell growth and proliferation

Midkine overexpression is implicated in promoting cancer cell growth, survival, metastasis and the formation of blood vessels to support the tumour. Furthermore, high levels of Midkine expression have been implicated in the development of cancer resistance to chemotherapy.

Figure 3: Midkine activates a number of pathways implicated in cancer progression



Source: Neumaier EE et al. The role of MDK in health and disease. Front Immunol. 2023 Nov 30

Inhibiting activity of Midkine is a promising therapeutic approach

Given the role of Midkine in driving cancer growth, Roquefort is developing medicines which aim inhibit the activity of the protein. This represents a promising approach to treatment. To our knowledge there are no therapies which target Midkine and very few competitors in this area. A search on ClinicalTrials.gov, generated only seven trials evaluating Midkine. Developing Midkine targeting therapies represents an attractive commercial opportunity given the lack of competition and a wealth of academic data generated by Lyramid regarding the therapeutic potential of the molecule.

…however, there are no approved drugs which target Midkine

Figure 5: MDK has been shown to be upregulated in various pathological conditions

Source: Neumaier EE et al. The role of MDK in health and disease. Front Immunol. 2023 Nov 30

1. Midkine antibody programme

Roquefort is progressing development of antibody-based therapies which were acquired as part of the Lyramid transaction. These antibodies target Midkine and aim to treat solid cancers characterised by high levels of Midkine expression. Roquefort is focusing on two antibodies, ROQA1 and ROQA2, which selectively bind to different regions of the Midkine protein.

- **ROQ-A2 (CAB-101)** binds to the C-domain of Midkine which is crucial for receptor interaction, angiogenesis (blood vessel formation), and immune modulation.
- **ROQA1 (CAB-102)** binds to the N-domain of Midkine which is primarily involved in promoting cell growth, survival and migration.

Roquefort has generated preclinical proof of concept for the Midkine antibody programme and has struck two commercial deals

Promising *in vivo* efficacy with a good safety profile

Roquefort and previously Lyramid, have conducted several *in vitro* and *in vivo* efficacy and toxicology studies on these Midkine antibodies. The studies have shown that the antibodies are effective in targeting several diseases characterised by high Midkine expression with an acceptable safety profile.

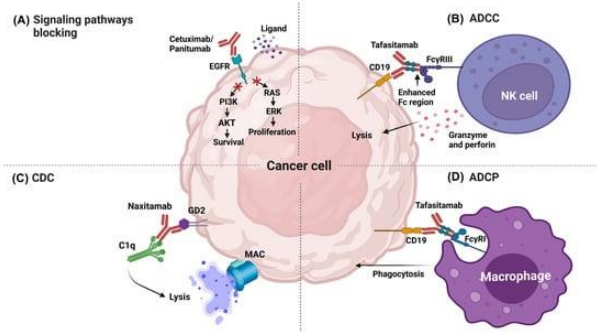
Recent commercial deals validate business model

Roquefort has struck two commercial agreements related to this programme: a licence agreement (subject to final due diligence) with PDC-CRO and an agreement with Randox Laboratories. The deals demonstrate the ability of the management team to strike commercial agreements and validates the Group's business model of developing its assets to key milestones, such as preclinical proof of concept, before looking to strike licensing deals for subsequent development.

Antibody method of action

Antibodies are proteins produced by white blood cells (B cells) and bind to specific antigens expressed on pathogenic cells and viruses. Antibody-based therapies can be designed to target specific antigens, such as Midkine, which are expressed on cancerous cells. Once bound to antigens, antibodies recruit other cells of the immune system to eliminate the target.

Figure 6: Antibody-based therapy mechanism of action



Source: Rodríguez-Nava, C., et al. (2023). Mechanisms of Action and Limitations of Monoclonal Antibodies in the Treatment of Cancer. Biomedicines, 11(1610).

Licencing Deals for therapeutics and diagnostics

Roquefort has struck two agreements related to the Midkine-antibody programme. These agreements are a validation of the Group's focus on Midkine as a therapeutic and diagnostic target and highlights the ability of the Group to strike commercial deals.

Midkine Antibody Licencing Deal with PDC-CRO

Roquefort recently signed a term sheet to out licence its Midkine antibody portfolio to PDC-CRO, a clinical research organisation based in the Middle East and Africa region.

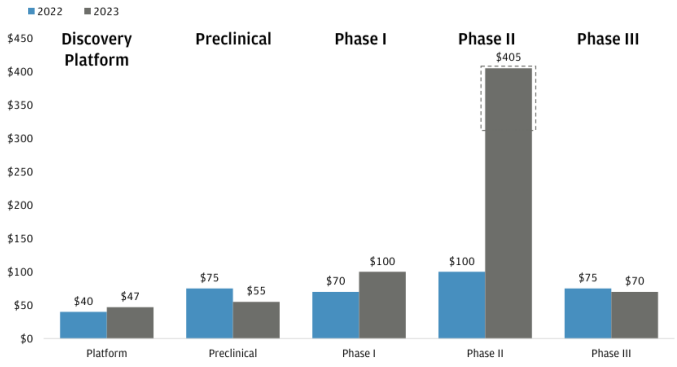
PDC license agreement could generate $10m upfront consideration and c.$50m should the SPV be sold after positive Phase 1 data

The agreement, subject to signing of a definitive licence agreement, places the Midkine antibody assets into a special purpose vehicle (SPV). Roquefort will grant a 20-year exclusive worldwide licence to the SPV. In return, Roquefort is eligible for $10m initial consideration, including non-dilutive equity in the SPV, a 24% share of any future trade sale proceeds of the SPV and anticipates an upfront cash component ranging between $1.2-2.5m. Roquefort Therapeutics is now working with PDC-CRO to complete due diligence and the drafting of the definitive licence agreement.

Scope for significant upside if positive Phase 1 data is generated

PDC-CRO expects to develop at least one of the Midkine antibodies within the SPV to the completion of a Phase 1 trials with a view to complete a trade sale. Should the partners compete a Phase 1 trial, management expects the 24% stake in the SPV to be worth up to us$50M (gross) based on similar trade sales. This is corroborated by industry data showing that the median upfront component for deals struck at Phase 1 is c.$100m (Source: Dealforma). This excludes additional conditional milestone or royalty payments.

Figure 7: In-licensing by big pharma: Median upfront cash & equity by stage at signing



Source: Dealforma/JP Morgan 2023 Annual Biopharma Licensing and Venture Report

Randox Licence Agreement worth up to £5m

Randox agreement provides potential diagnostics royalty stream expected in 2025

Last year, Roquefort Therapeutics struck an exclusive licence and royalty agreement with Randox Laboratories Ltd (Private), a leading diagnostics company. Roquefort has granted Randox an exclusive worldwide licence (excluding Japan) to utilise its Midkine antibodies in the field of medical diagnostics for a period of ten years. As part of the agreement, the partners will engage in collaborative research programmes to identify new cancer diagnostics that could be treatable with Roquefort's Midkine therapeutics. Roquefort received an upfront payment of £0.2m with further milestone payments expected in 2024 and royalty payments expected to commence in 2025. Roquefort believes the total transaction value could exceed £5m.

Preclinical data on Midkine-antibody programme

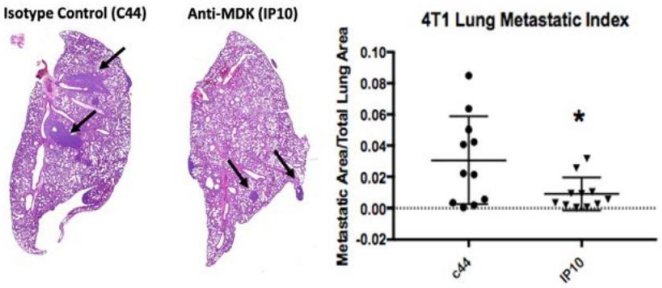
Roquefort is progressing development of the Midkine antibody programmes in collaboration with researchers at La Trobe University, Melbourne. The Group has generating encouraging preclinical data in several high-value disease areas. Humanised antibodies have been developed with both ROQA1 and ROQA2 shown to bind with high affinity to the Midkine protein. These antibodies have demonstrated significant anti-cancer activity in validated *in vivo* models of metastatic tumours and have also been shown to inhibit damaging inflammatory processes, particularly the recruitment and activation of neutrophils, which represses T regulatory cells.

Midkine antibodies have been shown to target the Midkine protein and have demonstrated efficacy in cancer models

Encouraging i*n vivo* safety data in metastatic lung and breast cancer

At the start of 2023, the Group announced positive *in vivo* safety data which evaluated the Midkine antibodies in animal models reflecting metastatic breast and lung cancers. The generation of initial safety data marks an important step in the preclinical development of the antibody programmes. The data is being used to guide further preclinical studies and potential future clinical testing.

Figure 8: Anti-MDK antibody reduces lung metastasis in breast cancer in vivo

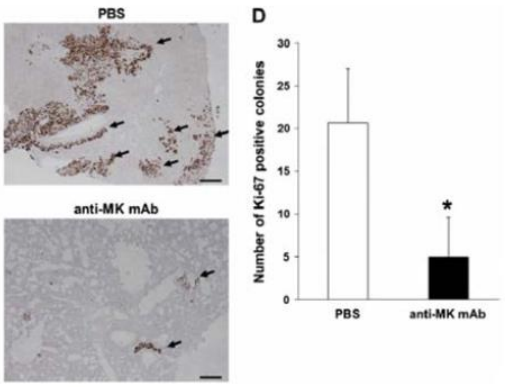


Source: Company Reports

Compelling *in vivo* efficacy data in Osteosarcoma

Following on from the safety data, the Group announced encouraging *in vivo* efficacy data from a study which evaluated the effectiveness of the antibodies in animal models of osteosarcoma, a rare form of cancer. ROQA2 was found to produce a statistically significant reduction in lung metastasis, and ROQA1 was found to reduce proliferation (growth rate) of the primary tumour.

Figure 9: IP14 completed GLP toxicology studies in two species & shows efficacy in osteosarcoma metastasis



Source: Company Reports

Eligibility for Orphan Drug Designation and expedited development

The generation of initial efficacy data marks an important step in the preclinical development of the Midkine antibody programme in an orphan indication. Given the small patient populations, regulators have put in place incentives to support the development of new treatments for rare (orphan) diseases, such as osteosarcoma.

Should Roquefort apply for, and receive, Orphan Drug Designation it would enable Roquefort to benefit from a suite of advantages in relation to the treatment's future development and market access for this indication. This includes potential tax credits, extended market exclusivity, eligibility for grants and an accelerated approval process. Qualification for this programme, or a similar programme in other jurisdictions, would significantly reduce the time and costs associated with the commercialisation of these assets.

Osteosarcoma overview

Osteosarcoma is a highly aggressive form of cancer which typically occurs in children and is associated with the over-expression of Midkine. Osteosarcoma arises from mutations in the osteoblasts, the cells responsible for bone formation. These genetic alterations lead to the uncontrolled proliferation of immature bone cells, which form tumours in the bone and can metastasise to other organs, most commonly the lungs.

Osteosarcoma is a rare cancer but represents the most common type of bone cancer in children and adolescents. In the US, c.800-900 new cases are diagnosed annually, accounting for about 2.3% of all childhood cancers. The five-year relative survival rate for localised osteosarcoma is 76%, but this rate drops significantly to 24% if the cancer has metastasised (spread) at the time of diagnosis (American Cancer Society). In the UK, osteosarcoma accounts for approximately 200-250 new cases per year with an overall five-year survival rate in the UK is approximately 55%. (Cancer Research UK).

Treatment of osteosarcoma is challenging due to its high potential for metastasis and resistance to conventional therapies. The current standard of care includes a combination of surgery and chemotherapy. Despite advances in surgical techniques and chemotherapy, the prognosis for patients with metastatic or recurrent osteosarcoma remains poor. Secondary osteosarcoma cases can be difficult to treat due to treatment resistance, with median survival for secondary osteosarcoma estimated to be around a year. This highlights the need for improved treatments which can offer a durable response. We would expect significant interest for Roquefort if it can replicate, in the clinic, the encouraging data generated in mouse models of which had developed resistance to an existing therapy.

2. Midkine therapeutic oligonucleotides

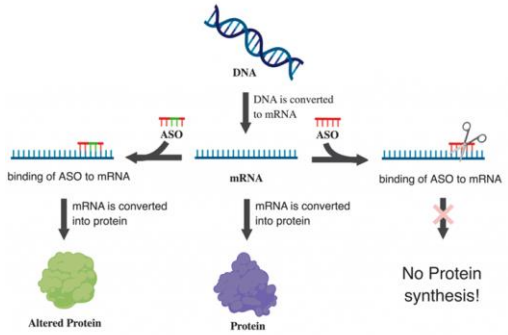
Roquefort is working with researchers at Australian medical research institutions to develop therapeutic oligonucleotides that reduce the expression and activity of the Midkine protein. Known as splice switching antisense oligonucleotides (SSOs), these are short single strands of nucleotides that are designed to bind to certain regions of pre-mRNA (immature mRNA) which encode for the Midkine protein.

Pre-mRNA is transcribed from DNA and is subsequently processed to remove non-coding regions, known as introns, and joining coding regions (exons) to generate mature mRNA that is used to direct protein synthesis. This process is known as RNA splicing.

Midkine mRNA has five exons, and Roquefort has designed four patent-protected SSOs that bind to Midkine pre-mRNA and leads to skipping of exons 3 or 4. This leads to the generation of incomplete Midkine mRNA. This incomplete mRNA is subsequently degraded or leads to the production of truncated, non-functional Midkine protein.

Midkine oligonucleotides disrupt RNA splicing and the production of functional Midkine protein

Figure 10: Oligonucleotides interfere with protein expression and activity

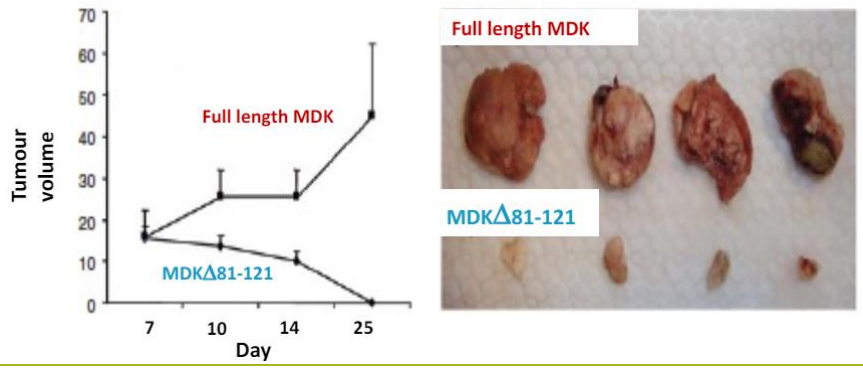


Source: National Ataxia Foundation, Larissa Nitschke, Created with BioRender.

SSOs lead to reduced Midkine expression and reduce tumour size

Researchers at Murdoch University have demonstrated that Midkine SSOs are highly effective in altering the splicing of Midkine mRNA, leading to a significant reduction in the production of the full-length, functional Midkine protein. This switch to the truncated Midkine is consistent with c.90% efficacy at the mRNA level. Furthermore, in *vivo* studies demonstrated that production of truncated Midkine has been shown to reduce the size of cancers. This data provides preclinical proof of concept regarding the use of SSOs to reduce tumour growth

Figure 11: Truncated MDK reduce tumour volumes in a validated animal model



Source: Company Reports

3. Midkine mRNA therapeutics

In March 2023, Roquefort Therapeutics announced it has developed a new platform of mRNA-based anti-cancer therapeutics. The platform consists of four mRNA constructs which target the expression of Midkine. The Company is now working towards demonstrating preclinical efficacy of the mRNA therapeutics in specific cancer indications.

mRNA leads to expression of nonfunction Midkine and reduced activity

Roquefort has developed mRNA molecules that encodes for non-functional truncated forms of the Midkine protein. Presence of this mRNA leads to the expression of non-functional Midkine protein that still binds to tumour receptors expression, however, does not initiate downstream signalling activity. Similar to the Midkine oligonucleotide programme, the presence of non-functional Midkine proteins leads to competition with functional Midkine for tumour binding sites and reduces activities such as promoting cancer cell growth, survival and metastasis.

Midkine mRNA therapeutics drive production of non-functional Midkine protein that reduces downstream signaling activity

New programme demonstrates ability to generate new assets in-house

The mRNA platform is the Company's fifth asset and the third as part of its Midkine programme, following the antibody and oligonucleotide programmes. The platform was developed internally, highlighting the Group's ability to generate new assets. This is also the Group's first mRNA-based candidate that targets Midkine, showing that Roquefort is leveraging the experience in mRNA therapeutic development from the acquisition of Oncogeni.

Preclinical data

In vitro data in breast and liver cancer

In June 2023, Roquefort Therapeutics announced positive results from *in vitro* studies evaluating the Group's anti-cancer mRNA therapeutics in breast and liver cancer. The studies, conducted at the University of Sydney, evaluated whether the mRNA constructs could slow cancer cell growth and migration (an early proxy for cancer metastasis) in *in vitro* models of breast and liver cancer. The studies demonstrated a statistically significant reduction in both cancer cell proliferation and migration.

Midkine mRNA therapeutics can be loaded onto lipid nanoparticle delivery systems and have shown anticancer activity in breast and liver cancer

Encouraging *in vivo* efficacy data in combination with lipid nanoparticle delivery system

In March 2024, Roquefort demonstrated that Midkine mRNA constructs loaded into a lipid nanoparticle delivery system demonstrated safety and efficacy in reducing functional Midkine in an *in vivo* model of liver cancer. The results, whilst early stage, provides preclinical evidence of efficacy of the mRNA programme.

An effective delivery system can be used to carry a nucleic acid payload to the target site of action. The use of lipid nanoparticles remains one of the most popular methods of nucleic acid delivery. Potential benefits include an improved safety and tolerability profile, a simple manufacturing process with rapid scale-up potential, and biological stability.

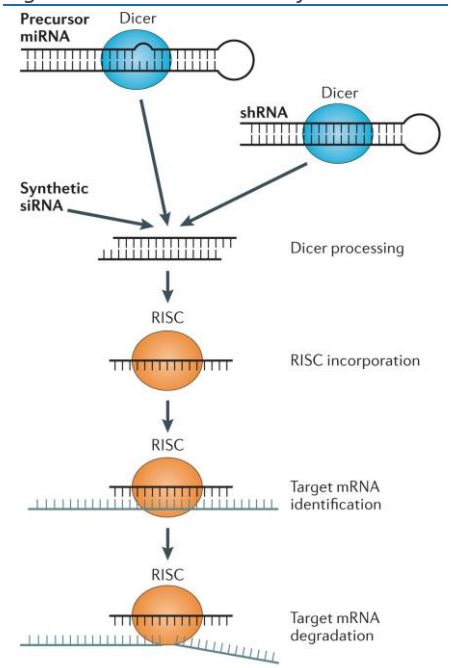
4. STAT-6 siRNA therapeutics

Alongside the Midkine programmes, Roquefort is also developing gene silencing therapeutics against STAT6 (signal transducer and activator of transcription 6), a protein overexpressed in a number of immunology and cancer indications.

Gene silencing is a proven method of treating disease

RNA interference is a natural biological process whereby small pieces of RNA (siRNA) inhibit protein translation by binding to, and degrading, specific sequences of mRNA. Degradation of mRNA subsequently inhibits expression of the target proteins. Roquefort has developed siRNAs which target the SH2 (Src-homology-2) domain of STAT6.

Figure 12: siRNA method of action



Source: Ghildiyal, M., Zamore, P. Small silencing RNAs: an expanding universe. Nat Rev Genet 10, 94–108 (2009). https://doi.org/10.1038/nrg2504

The Company'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 which target STAT6 mRNA and is currently evaluating these constructs in the lab.

STAT6 represents a validated target for immunology and cancer

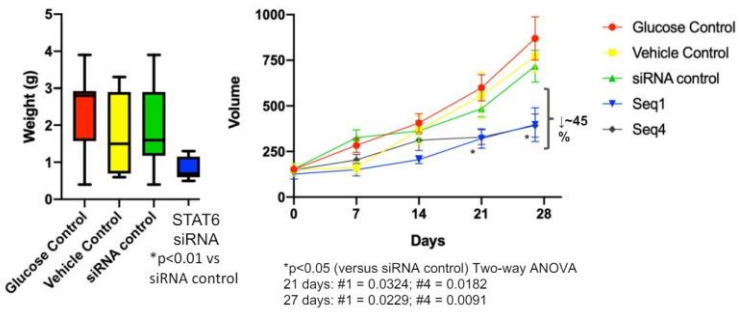
STAT6 is highly expressed in several cancer types, including prostate, colon and breast cancer. STAT6 regulates the expression of genes involved in immune response, cell survival, tumour proliferation and metastasis. High STAT6 expression is associated with cancer cell proliferation, increased malignancy and poor prognosis. There is considerable industry interest in STAT6. In 2023, Sanofi (SNA.EP) struck a deal with Recludix (Private) to licence a preclinical program targeting STAT6. The deal came with a US$125m upfront payment and potential milestone payments totalling $1.2bn.

Preclinical data

Anticancer effect demonstrated *in vivo* colorectal cancer model

STAT-6 targeting siRNA constructs have shown significant *in vivo* anti-cancer activity in validated models of colon cancer. STAT6 siRNAs demonstrated a significant reduction in the proliferation of colorectal cancer with an c.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 to 28 days.

Figure 13: Anti-STAT-6 siRNA showed significant anti-cancer activity in vivo



Source: Company Reports

Roquefort is conducting *in vitro* experiments on its STAT-6 siRNA programme in an immunology setting. Results from these experiments are expected in the short term and should support out-licencing discussions for this asset.

Nucleic acid treatments remain an area of industry interest

Nucleic acid-based therapeutics, such as siRNA, oligonucleotides and mRNA-based therapies, have several advantages over other approaches, such as a robust safety profile and a simple manufacturing process with rapid scale-up potential. Furthermore, as these therapeutics target gene expression rather than protein interactions, they may be able to inhibit targets which are thought to be 'undruggable' by protein and small-molecule treatments.

Considerable corporate activity for nucleic acid-based treatments

Nucleic acid-based treatments are attracting significant interest from industry. There have been several deals in the space driven by assets at the preclinical or early clinical stage. Deals usually consist of an upfront payment, conditional milestones, and options per target. These transaction highlights the potential deal structure that Roquefort could strike regarding its nucleic acid-based platforms.

Table 3: Nucleic acid focused deals

Year	Company	Company	Deal/agreement type	Upfront	Biodollars	Target / Disease Area	Stage at time of deal
July 2024	PeptiDream	Alnylam	Multi target collaboration	Undisclosed	$2.2bn	Undisclosed / Undisclosed	Preclinical
July 2024	Bicycle Therapeutics	Ionis	License & Collaboration	$45m	Undisclosed	TR1/Cardiovascular and Neurological	Preclinical
June 2024	Roche	Ascidian Tx	Multi target collaboration	$42m	$1.8bn	Undisclosed / CNS	Preclinical
June 2024	GSK	Elsie Biotech	Acquisition	$50m	Undisclosed	Undisclosed / Undisclosed	Preclinical
June 2024	Entos Pharma	Eli Lilly	Multi target collaboration	$50m	$400m	Undisclosed / Neurological	Preclinical
May 2024	Eli Lilly	Mina Tx	Multi target collaboration	$25m	$245m / target	Undisclosed / Undisclosed	Preclinical
April 2024	Boehringer Ingelheim	Ochre Bio	Multi target collaboration	$35m	$1bn	Undisclosed / NASH	Preclinical
April 2024	Ipsen	Skyhawk Tx	Multi target collaboration	Undisclosed	$1.8bn	Undisclosed / Undisclosed	Preclinical
March 2024	Novo Nordisk	Cardior	Acquisition	EUR1.025bn	NA	anti-miR-132 / Heart failure	CDR132L / Phase 2
January 2024	Boehringer Ingelheim	Suzhou Ribo Life Sciences	Multi target collaboration	Undisclosed	$2bn	Undisclosed / NASH	Preclinical
November 2023	BMS	Avidity Biosciences	Multi target collaboration	$100m	$2.175bn	Undisclosed / CVD	Preclinical
October 2023	GSK	Arrowhead	License & Collaboration	Undisclosed	$1bn	HPV / Hepatitis B	JNJ-3989 / Phase 3
September 2023	Pfizer	Ginkgo Bioworks	Multi target collaboration	Undisclosed	$331m	Undisclosed / Undisclosed	Preclinical
September 2023	Roche	Ionis	License & Collaboration	$60m	$60m	huntingtin / Alzheimer's disease and Huntington's	Tominersen / Phase 2
July 2023	Roche	Alnylam	Co-development & commercialisation	$310m	$2.8bn	AGT / Hypertension	Phase 2
July 2023	Novartis	DTx Pharma	Acquisition	$500m	Undisclosed	PMP22 / CNS	Preclinical
December 2022	Eli Lilly	ProQR Tx	Multi target collaboration	$75m	$3.75bn	Undisclosed / CNS	Preclinical
December 2022	GSK	Wave Life Sciences	Multi target collaboration	$170m	c.$1bn	AATD	WVE-006
January 2022	GenEdit	Sarepta Tx	Multi target collaboration	$57m	Undisclosed	Undisclosed / Neuromuscular	Preclinical
November 2021	Novo Nordisk	Dicerna	Acquisition	$3.3bn	Undisclosed	LDHA / Kidney disease	Phase 3
October 2020	Takeda	Arrowhead	License & Collaboration	$300m	$1.04b	Z-AAT / Liver disease	ARO-AAT / Phase 2
September 2020	Moderna	Vertex	License & Collaboration	$75m	$380m	CFTR/Cystic Fibrosis	Preclinical
March 2020	AstraZeneca	Silence Tx	Multi target collaboration	$80m	$400m/target	Undisclosed / liver, heart, lung	Preclinical
November 2019	Novartis	The Medicines Company	Acquisition	$9.7bn	Na	Inclisiran / heart disease	Phase 3
November 2019	Novo Nordisk	Dicerna	Multi target collaboration	$225m	$357m/target	Undisclosed / cardio-metabolic diseases	Preclinical

Source: Company websites

5. MK cell therapy with immunology and oncology applications

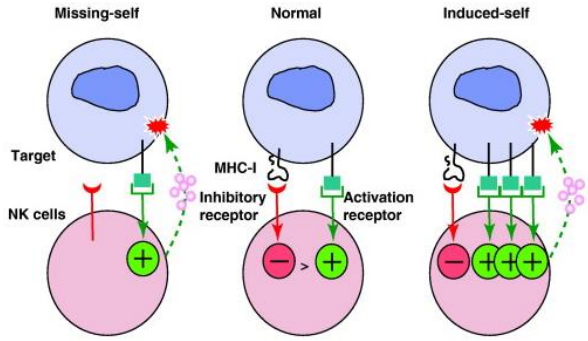
Alongside the nucleic acid and antibody-based platforms, Roquefort is progressing development of Mesodermal Killer (MK) cells. MK cells are a novel class of cell therapy which target diseased cells both directly and indirectly by enhancing the activity of other white blood cells.

Similar characteristics to NK cells but with a novel composition

MK cells can target cancer cells directly and indirectly by directing the immune system to attack the cell

MK cells were named after natural killer (NK) cells due to similar characteristics to NK cells. NK cells are a form of lymphocyte (white blood cell) that forms part of the innate immune system. NK cells detect and eliminate infected cells, pathogens and certain tumour cells. They are termed "natural" killers as they can target and eliminate pathogens without prior exposure to the pathogen. NK cell activity relies on recognising whether the pathogen or cell is deemed "self" (healthy) or "non-self" (diseased). This recognition relies on the presence or lack of the major histocompatibility complex class I (MHC I), a protein complex. If no MHC I is detected this leads to NK cell activation.

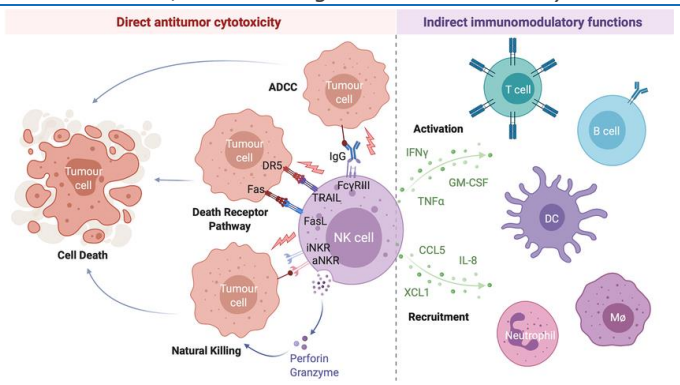
Figure 14: Natural Killer cells recognise potential pathogens via presence/lack of MHC I



Source: Unifying concepts of MHC-dependent NK cell education; Elliot, JM; Trends in Immunology (2011)

NK cells can treat cancer by directly killing cancer cells by releasing cytotoxic granules into the target cells or by releasing pro-inflammatory cytokines and chemokines to activate other immune cells to fight cancer. MK cells have been shown to demonstrate these characteristics, however, have a different composition to NK cells. MK cells are formed from engineered mesodermal cells derived from adult bone marrow. NK cells are derived from hematopoietic stem cells in the bone marrow.

Figure 15: Similar to NK cells, MK cells target cancer cells directly and indirectly



Source: Barnes et al. (2021). Making a Killer: Selecting the Optimal NK Cells for Improved Immunotherapies. Frontiers in Immunology

MK cells offer potential improvements to existing CAR-T cell therapy

Management believe that MK cells may have an improved profile compared to other cell therapies, such as CAR-T therapeutics. CAR-T therapies have shown significant improvement in patient survival across a number of blood malignancies. However, commercial uptake has been impacted by several challenges, including high cost of manufacturing, scalability and a high risk of an adverse immune response, such as cytokine release syndrome.

MK cells offer an alternate approach to CAR-T cell therapies including improved safety profile and reduced manufacturing costs

NK cells have been shown to overcome these challenges. Clinical studies which administered NK cells have shown reduced levels of inflammatory cytokines and cytokine release syndrome events when compared to CAR-T. NK cells can be delivered as an off-the shelf treatment which should ease manufacturing scale up activities and reduced associated costs. This should reduce end user costs when compared to list prices of approved CAR-T cell, which tend to range between $400-$600k. Given the similarities to NK cells, we believe MK cells should also benefit from these characteristics.

MK cells have a unique fingerprint

MK cells are identified by a fingerprint of seven cell surface receptors (Table 4) and the absence of three common cell surface receptors (CD34, CD45 and CD56). The seven receptors confer different characteristics in supporting anticancer activity.

Table 4: MK cells have a unique antigen fingerprint

Receptor	Function	Role in NK Cells
CD16	Low-affinity receptor for the Fc portion of IgG antibodies	Crucial for Antibody-Dependent Cellular Cytotoxicity (ADCC); binds to antibodies on target cells, triggering cytotoxic granule release and target cell lysis
CD96	Adhesion receptor involved in NK cell-target cell interactions	Mediates interactions with tumour cells; can act as both an activating and inhibitory receptor, influencing NK cell adhesion, cytokine production, and cytotoxicity
CD112	Ligand for DNAM-1 (CD226) and TIGIT receptors	Promotes NK cell adhesion, activation, and cytotoxicity when bound to DNAM-1; can inhibit NK cell functions when interacting with TIGIT
CD137L	Ligand for the costimulatory receptor CD137 (4-1BB)	Enhances NK cell proliferation, survival, and cytotoxic activity upon binding to CD137, providing costimulatory signals important for NK cell activation
CD178	Binds to Fas receptor (CD95) on target cells	Induces apoptosis in Fas-expressing target cells through the extrinsic apoptotic pathway, contributing to NK cell-mediated cell death
CD253	Binds to death receptors DR4 and DR5 on target cells	Triggers apoptosis in target cells via the extrinsic pathway, enhancing NK cell-mediated cytotoxicity against tumour and infected cells
CD277	Member of the butyrophilin family involved in immune regulation	Influences NK cell function and immune responses; involved in the recognition of phosphoantigens and modulation of NK cell activity

Source: Company reports

Preclinical data

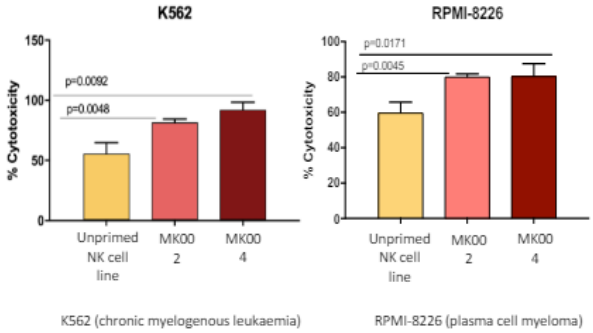
In vitro activation of NK cells across three cancer types

In September 2023 Roquefort Therapeutics announced encouraging preclinical data from its MK cell programme. MK cells were tested in combination with NK cells in three cancer types (ovarian cancer, acute myeloid leukaemia, multiple myeloma).

MK cells were shown to activate natural killer cells, and this activation produced up to a two-fold increase in cytotoxicity compared to treatment with NK cells alone. The data, whilst early stage, indicates how the MK programme can be used to activate natural killer cell in three difficult to treat cancer types.

MK cells can activate NK cells to target cancer cells as well as directly targeting the tumour

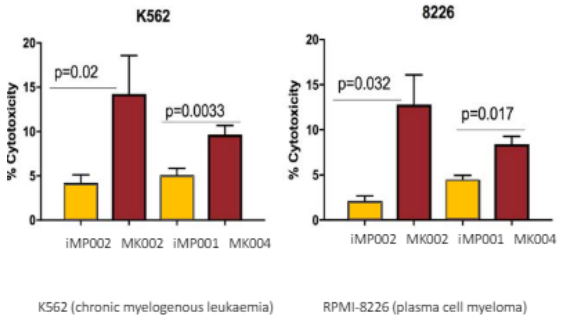
Figure 15: MK cell types were able to prime of NK cells in vitro to target blood cancer cells



Source: Company Reports

MK cells were also shown to directly target and eliminate blood cancer cells. This demonstrates the dual action approach of how MK cells can be used to treat blood malignancies.

Figure 16: MK cell types were able to target blood cancer cells in vitro via direct cytotoxicity



Source: Company Reports

Future development plans and positioning

The Company now plans to complete *in vivo* studies to further demonstrate in animal models how MK cells can drive NK cell activation in immunology and cancer. A potential clinical study could investigate the activity of MK cells either as a monotherapy or in combination with a targeted therapy in an immunology and / or oncology setting.

Cell therapy continued industry interest in preclinical stage companies

There remains considerable interest in cell therapies with multiple agreements being struck at different stages of development. Recent deals include the $1.2bn acquisition of Gracell Biotechnologies (GRCL.NQ), a clinical stage cell therapy business, by AstraZeneca (AZN.L) in December 2023. Gracell's lead product, GC012F, is a CAR-T cell therapy currently being evaluated in a Phase 1b/2 trial in patients with relapsed or refractory multiple myeloma, a blood disease. This transaction demonstrates the scope for agreements to be struck at an early clinical stage. Should Roquefort generate positive preclinical or early clinical data, this should put the Group in a good position to initiate discussions with potential partners.

Furthermore, the recent IPO of Artiva Biotherapeutics (ARTV.NQ), a developer of NK therapies demonstrates investor appetite. Artiva raised $167m as part of the IPO, which is supporting clinical development of its lead asset, AlloNK, which is currently undergoing Phase 1 trials.

Table 5: Selected cell therapy deals

Year	Company	Company	Deal type	Upfront	Biodollars	Target / Disease area	Lead asset stage at time of deal
February 2024	Autolus	BioNTech	Collaboration	$50m upfront + $200m investment	undisclosed	CLDN6+ tumours	Phase 1
February 2024	Astellas Pharma	Kelonia Therapeutics	Collaboration & License	$40m	$800m	Undisclosed / Immune/oncology	Preclinical
January 2024	AbbVie	Umoja Biopharma	Collaboration & License	Undisclosed	$1.4b	CD19+ Blood malignancies	Preclinical
January 2024	Precision BioSciences	TG Therapeutics	License Agreement	$17.5m	$288m	BCMA /B-cell diseases	Preclinical
August 2023	Precision BioSciences	Imugene Limited	License Agreement	$21m	$145m	BCMA /B-cell diseases	Preclinical
December 2022	Gilead	Tmunity	Acquisition	Undisclosed	Undisclosed	PSMA / prostate cancer	Phase 1
December 2023	AstraZeneca	Gracell	Acquisition	$1bn	$200m	BCMA / Blood malignancies	Phase 1b/2
May 2023	Cellular Biomedicine	Johnson & Johnson	Collaboration & License	$245m	undisclosed		Phase 1b
August 2023	Poseida Therapeutics	Roche	Collaboration & License	$110m	$6b	BCMA / Blood malignancies	Phase 1
October 2022	Autolus	BMS	Collaboration & License	Undisclosed	Undisclosed	Undisclosed	Preclinical
June 2022	Immatics	BMS	Multi-target collaboration	$60m	$700m per programme	Undisclosed	Preclinical
September 2022	Arsenal Biosciences	Roche	Collaboration	$70m	Undisclosed	Undisclosed	Preclinical
June 2022	Galapagos	CellPoint	Acquisition	EUR125m	EUR114m	Leukaemia	Phase 1/2a
October 2021	Gammadelta	Takeda	Acquisition	Undisclosed	Undisclosed	Blood malignancies	Phase 1
April 2020	Johnson & Johnson	Fate Therapeutics	Collaboration & License	$50m	up to $1.8bn	Undisclosed	Phase 1
March 2020	Servier	Cellectis	License Agreement	$28m	$410m	CD19+ Blood malignancies	Phase 1
November 2020	Kiadis	Sanofi	Acquisition	$268m	None	Leukaemia	Phase 2
April 2020	Johnson & Johnson	Fate Therapeutics	Collaboration & License	$50m	$1.8bn	Undisclosed	Preclinical

Source: Company websites

Financials

Income Statement (£m)

Fiscal Year	2021A	2022A	2023A
Fiscal Period end date	31/12/2021	31/12/2022	31/12/2022
Revenue	0.00	-	0.20
Other Income	0.00	-	-
COGS	(0.01)	-	-
Administrative expenses	(0.25)	(1.31)	(1.50)
R&D expenses	-	(0.32)	(0.62)
Share based payments	(0.25)	(0.01)	(0.01)
IPO and acquisition costs	(0.41)	-	-
Operating profit	**(0.92)**	**(1.63)**	**(1.93)**
Interest receivable	-	-	0.00
Interest payable	-	-	(0.00)
Depreciation	-	-	(0.00)
Profit before tax	**(0.92)**	**(1.63)**	**(1.93)**
Income tax credit (expense)	-	0.02	0.19
Profit after tax	**(0.92)**	**(1.62)**	**(1.74)**
Comprehensive income/(loss) to the year	**(0.92)**	**(1.62)**	**(1.74)**
Weighted average number of ordinary shares in issue	103.48	103.48	129.15
EPS	(0.89)	(1.56)	(1.35)

Source: Company announcements, SP Angel estimates

Cash flow (£m)

Fiscal Year	2021A	2022A	2023A
Fiscal Period end date	31/12/2021	31/12/2022	31/12/2022
Profit before tax	**(0.92)**	**(1.63)**	**(1.93)**
Depreciation & Amortisation	-	0.00	-
Foreign exchange gain	0.00	(0.01)	0.03
Interest income	-	-	(0.00)
Interest expense	-	-	0.00
Taxation	-	0.02	0.19
Share based payments	0.37	0.01	0.01
Other non-cash items	(0.00)	-	-
Changes in working capital	**0.10**	**0.04**	**(0.03)**
Net cash used in operating activities	**(0.46)**	**(1.57)**	**(1.74)**
Proceeds from issuance of equity securities	2.18	3.12	-
Share issue costs	(0.16)	(0.02)	-
Interest paid	-	-	(0.00)
Net cash flow generated from financing activities	**2.02**	**3.10**	**(0.00)**
Interest income		-	0.00
Purchase pf PPE		-	(0.05)
Acquisition of subsidiary, net of cash acquired	(0.61)	(0.10)	-
Net cash flow generated from (used in) investing activities	**(0.61)**	**(0.10)**	**(0.05)**
Net increase/(decrease) in cash and cash equivalents	0.96	1.43	(1.79)
Cash and cash equivalents at the beginning of the period	**-**	**0.90**	**2.32**
Cash and cash equivalents at the end of the period	**0.96**	**2.32**	**0.53**

Source: Company announcements, SP Angel estimates

SP Angel | Prince Frederick House | 35-39 Maddox Street | London | W1S 2PP | United Kingdom

Balance sheet (£m)

Fiscal Year	2021A	2022A	2023A
Fiscal Period end date	31/12/2021	31/12/2022	31/12/2022
PPE	-	-	0.05
Intangible assets	1.48	5.34	5.34
Non-current assets	**1.48**	**5.34**	**5.39**
Trade and other receivables	2.18	0.10	0.16
Cash and cash equivalents	0.90	2.32	0.54
Current assets	**3.08**	**2.42**	**0.69**
TOTAL ASSETS	**4.56**	**7.77**	**6.09**
		-	-
Share capital	0.72	1.29	1.29
Share premium	3.46	4.40	4.40
Other reserves	0.37	0.36	0.40
Merger relief reserve	0.45	3.70	3.70
Retained Earnings	(0.91)	(2.55)	(4.29)
TOTAL EQUITY	**4.08**	**7.21**	**5.50**
Trade and other payables	0.20	0.28	0.31
Current liabilities	**0.20**	**0.28**	**0.31**
Non-Current liabilities	**0.28**	**0.28**	**0.28**
TOTAL LIABILITIES	**0.48**	**0.56**	**0.59**
EQUITY + LIABILITIES	**4.56**	**7.77**	**6.09**

Source: Company announcements, SP Angel estimates

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Key risks

As an early-stage healthcare company Roquefort is exposed to risks inherent to the sector. Of these potential risks, development risk and the regulatory pathway and are the most relevant to the Group.

Preclinical developmental risk

As a preclinical company Roquefort has not yet generated human data using its product candidates. Preclinical testing can be lengthy and uncertain and there is no guarantee that Roquefort will receive IND-approval from the regulator to test their products in humans. Candidates may be subject to delayed entry into clinical trials or may not progress to the clinic. There is no guarantee that results in preclinical tests will be replicated in humans.

Clinical trial risk

The outcome of clinical trials cannot be pre-determined and there is no guarantee that any future clinical trial conducted by Roquefort will meet the primary endpoint. The Company's development programmes are always at risk of termination should any future trial raise any concerns about a product's safety or efficacy. Clinical trials may raise safety issues and there may be requests for additional clinical data by the FDA. Both of these possibilities would require additional working capital.

Regulatory risk

There is no guarantee that Roquefort will receive marketing approval for its proposed treatments and a delay or failure to receive marketing approval could have a negative impact on the Company's operation.

Commercial risk

Potential commercial uptake of the Company's products may be slower than expected and there is no guarantee that the Group will successfully partner its assets.

Key personnel

The loss of personnel may have a negative impact on the Company's strategy and ability to achieve future milestones.

Financial Risk

To fund its ongoing operations, we expect the Company to require additional capital over the coming years.

Key Management

Stephen West - Executive Chairman

Stephen is a Fellow Chartered Accountant with over 30 years of financial and corporate experience gained in public practice, the resource sector, life sciences and investment banking. Stephen has a proven track record in working with growth companies with extensive experience in IPOs, secondary listings, corporate finance, fundraising an investor relation. Stephen is currently a non-executive director of EnergyPathways plc (AIM:EPP).

Ajan Reginald - Chief Executive Officer

Ajan is an experienced biotechnology CEO with a track record in drug development, biotech transactions and commercialisation. Over 20 years, he has served as the Global Head of Emerging Technologies for Roche Group (ROG.SWX), Chief Operating Officer and Chief Technology Officer of Novacyt S.A (NCYT.L), Boston Consulting Group and CEO of Celixir Ltd. With Prof. Sir Martin Evans, Ajan founded Celixir and developed a novel cardiac cellular medicine which completed pre-clinical development and won FDA, MHRA and EU regulatory trial approvals. Celixir completed a licensing for the Japan market only with Daiichi Sankyo, a Japanese Big Pharma company which included a £12.5m upfront payment and a £5m equity investment which valued Celixir at £220m. Ajan is an alumni of Harvard Business School (AMP) , Fulbright Scholar and a graduate of the University of Oxford (MSc Experimental Therapeutics), Kellogg Business School (MBA) Northwestern University and University of London (BDS).

Professor Sir Martin Evans, Nobel Laureate - Non-Executive Director

Sir Martin was the first scientist to identify embryonic stem cells, which can be adapted for a wide variety of medical purposes. In 2007, he was awarded the Nobel Prize for Medicine, the most prestigious honour in world science, for these “ground-breaking discoveries concerning embryonic stem cells and DNA recombination in mammals.” Sir Martin has published more than 120 scientific papers. He was elected a Fellow of the Royal Society in 1993 and is a founder Fellow of the Academy of Medical Sciences. He was awarded the Walter Cottman Fellowship and the William Bate Hardy Prizes in 2003 and in 2001 was awarded the Albert Lasker Medal for Basic Medical Research in the US. In 2002 he was awarded an honorary doctorate from Mount Sinai School of Medicine in New York, regarded as one of the world's foremost centres for medical and scientific training. He has also received honorary doctorate awards from the University of Bath, University of Buckinghamshire, University College London, University of Wales and the University of Athens. Sir Martin gained his BA in Biochemistry from Christ College, University of Cambridge in 1963. He received an MA in 1966 and a DSc in 1966. In 1969 he was awarded a PhD from University College, London. He joined the Cardiff University School of Biosciences in 1999. He was knighted in 2004 for his services to medical science and in 2009 was awarded the Gold Medal of the Royal Society of Medicine in recognition of his valuable contribution to medicine. In 2009 he also received the Baly Medal from the Royal College of Physicians and the Copley Medal, the Royal Society's oldest award, joining an eminent list of previous recipients including Albert Einstein.

Darrin Disley - Non-Executive Director

Darrin is a renowned scientist, entrepreneur, angel investor and enterprise champion who has started, grown, or invested in over 40 start-up life science, technology and social enterprises, raising US$600 million in business financing and closing US$700 million in commercial deals. He was CEO of Horizon Discovery Group plc for 11 years, during which he led the company from start-up through a US$113 million IPO, and rapid scale-up powered by multiple acquisitions of US peer companies to become a global market leader in gene editing and gene modulation technologies. He was awarded a lifetime Queen's Award for Enterprise Promotion in 2016 for his work in promoting enterprise across the UK and appointed OBE in 2018 for his services to business and enterprise in the healthcare sector.

Jean Duvall - Non-Executive Director

Jean 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 $2bn 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).

Simon Sinclair - Non-Executive Director

Simon is a senior executive physician scientist with over 20 years' pharma, medtech and consumer healthcare industry experience. He is the former Chief Safety Officer at Reckitt Benckiser and was previously at Johnson and Johnson Medical Devices, first as International Clinical Director, then leading Medical Affairs for its EMEA region. Prior to this, Simon led translational medicine efforts and the early clinical development at Merck and Co (MSD) in the USA. Originally trained as an ophthalmologist, Simon holds a medical degree and a PhD in neural transplantation from the University of Cambridge. Simon is currently a non-executive director of Ondine Biomedical Inc. (AIM:OBI) and a non-executive director at Renovos Biologics Limited.

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SP Angel acts as as Broker to Roquefort Therapeutics

Recommendations are based on a 12-month time horizon as follows:

Buy - Expected return >15%
Hold - Expected return range -15% to +15%
Sell - Expected return < 15%