Roquefort Therapeutics PLC

Progress of Midkine RNA oligo program

22 June 2023

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RNA oligonucleotide program shows in vitro anti-cancer efficacy

Roquefort Therapeutics today announced the progress of its anti-cancer RNA oligonucleotide programs targeting Midkine expressing cancers, producing >90% in vitro efficacy (at the mRNA level) in human liver and neuroblastoma cancer cells.

This work has been conducted through strategic research partnerships at the Faculty of Medicine and Health at the University of Sydney and the Immune Oncology Laboratory at the School of Biomedical Sciences, University of New South Wales (UNSW). The team led by Professor Mark Molloy at the University of Sydney detected a novel peptide corresponding to the truncated Midkine protein from cancer cells. This in vitro proof-of-concept study confirmed that the Company's novel antisense oligonucleotides (ASO) produced a novel non-functional Midkine protein. Non-functional Midkine protein has been shown to produce >90% in vitro efficacy (at the mRNA level) in human liver cancer and neuroblastoma cancer cells.

The UNSW team led by Scientia Associate Professor Orazio Vittorio and Dr. Filip Michniewicz has continued this line of research to evaluate the optimal combination of oligonucleotides in an in vitro model of hepatocellular carcinoma (HCC) liver cancer. A proprietary combination of the Company's oligonucleotides demonstrated in vitro efficacy in HCC cells producing a significant reduction in full length Midkine and generated a novel non-functional Midkine.

The Company's anti-cancer RNA oligonucleotide program will now progress into in vivo studies which are planned to complete in Q4 2023.

Synergistic Midkine programs: Roquefort's proprietary combination of oligonucleotides attack a different Midkine region versus the antibodies and mRNA. This diversity of targeting regions may be helpful in developing mono or combination therapies.

Liver cancers and HCC: Liver cancer is the 6th most common cancer worldwide, with 830,180 deaths in 2020 according to World Cancer Research Fund International. HCC is the fourth-leading cause of cancer mortality worldwide and accounts for circa 90% of liver cancers. Because of the limited efficacy of conventional therapy , the 5-year survival rate is just 21% (American Cancer Society). The global liver cancer drug market estimated at US$2.4bn in 2022 is projected to reach US$9.3bn by 2030, at a CAGR of 18.6% according to the market research firm Research And Markets in February 2023.

Key Statistics:

Code	ROQ
Listing	LSE; OTCQB
Sector	Biopharma
Market cap*	£9.0m
Shares in issue*	129.15m
Current price*	7p
12-month high/low*	9p/6.375p
Free float**	55%

**Closing price on 21 June 2023. High/low based on closing prices. **Free float based on Hybridan estimates.*

Share Price Performance

Year to date	8%
Past 12 months	-19%
2021	75%

Source: Alpha Terminal

Financials Y/E Dec (£)

	Sales	EBIT	Net cash
2021	719	(917,433)	899,721
2022	-	(1,634,303)	2,322,974

Source: Company Data

Company Description

Roquefort Therapeutics is a drug and therapy discovery and development company for hard-to-treat cancers focusing on novel targets. All of its development programs are supported with licensed patents and anchored on Roquefort's own knowhow and intellectual property.

Roquefort has five best-in-class oncology drug development programs: (1) Midkine antibodies; (2) Midkine RNA oligonucleotide therapeutics with novel anti-cancer gene editing action; (3) Midkine mRNA program; (4) Mesodermal Killer (MK) cell therapy with direct and nature-killer-mediated anti-cancer action; and (5) siRNA targeting novel STAT-6 target in solid tumours.

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Roquefort's anti-cancer RNA oligonucleotide programs

Midkine, a heparin-binding protein, has long been known to be important in embryonic development. While barely detectable in healthy adults, Midkine is highly expressed during oncogenesis, the process through which healthy cells develop into cancer cells. Midkine hinders the normal immune response to tumours and promotes metastatic spread to other organs, thereby contributing to various levels of cancer progression and reduced patient survival.

Roquefort believes its knowhow and patent strategy (the combination of the exclusive license and the efforts to patent in-house R&D) have established the entry barrier in targeting Midkine.

In March 2022, Roquefort announced that it had filed its first composition of matter patent application, covering ASO drugs to block the action of Midkine. This patent aims to protect the IP and the potential value of this new class of RNA therapeutic drug. Subsequent methods patents will later be filed to provide additional IP protections, such as covering the use of the Midkine ASO in different clinical indications.

Mechanism of action of ASO and potential in liver disease treatments

The ASO approach to cancer is different from and hence complementary to the antibodies approach and the mRNA approach.

Antisense agents are synthetic, single-stranded short sequences of DNA bases designed to hybridise to specific sequences of messenger RNA (mRNA) forming a duplex. Antisense agents can be specifically targeted to genes that control expression of antibiotic resistance mechanisms, thereby potentially restoring an antibiotic-sensitive phenotype to the cell. Antisense therapy is highly specific to the target and can produce a lasting clinical effect.

ASO can regulate the proliferation, migration, and invasion of tumour cells, as well as regulate immunity and liver metastasis. The paper by Kailing Lu et al. published on Frontier in Pharmacology in 2022 specially describes why ASO is a promising intervention for liver diseases by functioning mainly through four mechanisms: (1) affecting of mRNA maturation; (2) selective regulating of the splicing of precursor mRNA; (3) activation of the RNase H enzyme to degrade DNA-mRNA duplexes through cleavage; and (4) prevention of interaction of RNA and ribosome through steric hindrance, blocking the translation process.

It is important to note that ASO drugs have different absorption and metabolism pathways than traditional small molecule drugs. ASO drugs are administered mainly by intravenous and subcutaneous routes. When they enter the body, they are mainly

degraded by endonucleases and exonucleases in the blood and target organs and hence not metabolised by the liver and hepatic microsomes.
(https://www.frontiersin.org/articles/10.3389/fphar.2022.1061842/full)

Global ASO therapeutics market

The global ASO therapeutics market size is valued at US$27.0bn in 2022 and is predicated to reach US$80.8bn in 2031, at a CAGR of 13.2% according to InsightAce Analytics.

It is worth noting that ASO therapeutics are mainly used for neurodegenerative disorders today. The growth in the oncology segment is expected to be driven by treatment for prostate cancer.

Financial Statements

Income Statement (£) Y/E December	2021	2022	Notes
Revenue	719	-	
Other income	130	-	
Cost of goods	(10,069)	-	
Administrative expenses	(252,392)	(1,306,561)	Director and employee costs and other expenditures
Costs associated with the IPO	(182,053)	-	
Share based payments	(248,326)	(8,427)	
Costs associated with acquisition	(224,744)	-	
Research and development expenditure	(698)	(319,315)	
Amortisation of Intangible assets	-	-	
Operating loss	(917,433)	(1,634,303)	
Finance income	-	-	
Profit (loss) before tax	(917,433)	(1,634,303)	
Taxation	-	18,886	
Profit (loss) for the period	(917,433)	(1,615,417)	
Other comprehensive loss	624	(14,989)	
Total comprehensive income (loss)	(916,809)	(1,630,406)	
Earnings (loss) per share	(3.71)	(1.56)	
Weighted average number of shares	24,701,793	103,479,476	
Balance Sheet (£) Y/E December	**2021**	**2022**	
Intangible assets	1,481,530	5,343,505	Including £5,061,594 in-progress R&D
TOTAL NON-CURRENT ASSETS	1,481,530	5,343,505	Including goodwill of £281,911
Trade and other receivables	2,178,783	101,738	2021 receivable due to shares issued to acquire Lyramid
Cash and cash equivalents	899,721	2,322,974	
TOTAL CURRENT ASSETS	3,078,504	2,424,712	
TOTAL ASSETS	4,560,034	7,768,217	
Deferred tax liabilities	281,911	281,911	
TOTAL NON-CURRENT LIABILITIES	281,911	281,911	
Trade and other payables	195,517	279,670	
TOTAL CURRENT LIABILITIES	195,517	279,670	
TOTAL LIABILITIES	477,428	561,581	
Share capital	719,000	1,291,500	
Share premium	3,460,595	4,403,094	£3.75m equity consideration for acquisition of Oncogeni
Share based payments reserve	366,708	375,135	
Merger relief reserve	450,000	3,700,000	Including £3,250,000 due to acquisition of Oncogeni
Retained deficit	(914,321)	(2,548,728)	
Currency translation reserve	624	(14,365)	
TOTAL EQUITY	4,082,606	7,206,636	
TOTAL LIABILITIES AND EQUITY	4,560,034	7,768,217	

Source: Company Data

Cash Flow Statement (£) Y/E December	**2021**	**2022**	
Profit (loss) before tax	(996,068)	(1,634,303)	
Adjustment for:			
Foreign exchange	765	(9,918)	
Non-cash adjustment	(2,602)	-	
Share based payment	366,708	8,427	
Taxation	-	18,886	
Changes in working capital:			
Change in trade and other receivables	(24,434)	(20,318)	
Change in trade and other payables	129,525	59,750	
Change in inventory	9,273	-	
CASHFLOWS FROM OPERATING ACTIVITIES	(516,833)	(1,577,476)	
Acquisition of subsidiary, net of cash acquired	(606,226)	(103,478)	-
CASHFLOWS FROM INVESTING ACTIVITIES	(606,226)	(103,478)	-
Proceeds from issue of ordinary shares	2,182,798	3,121,202	£2m received in Jan 2022 +£1m in Sep 2022
Share issuance costs	(159,405)	(18,990)	
CASHFLOWS FROM FINANCING ACTIVITIES	2,023,393	3,102,212	
Net change in cash & cash equivalents	900,335	1,421,258	
FX translation difference	(614)	1,995	
Cash at the beginning of the period	-	899,721	
Cash at the end of the period	899,721	2,322,974	

Source: Company Data

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