22 June 2023

Roquefort Therapeutics plc

("Roquefort Therapeutics" or the "Company")

RNA Medicine Shows In Vitro Anti-Cancer Efficacy

Further preclinical progress

Roquefort Therapeutics (LSE:ROQ), the Main Market listed biotech company focused on developing first-in-class medicines in the high value and high growth oncology market, is pleased to announce the progress of its anti-cancer RNA oligonucleotide program targeting Midkine expressing cancers producing >90% *in vitro* efficacy (at the mRNA level) in human liver and neuroblastoma cancer cells.

Following the announcement on 5 December 2022 of the Company's presentation of its Midkine RNA oligonucleotide program results at the European Society of Medical Oncology Asia conference, the development of its oligonucleotide portfolio has continued. 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 experiment utilised advanced proteomic analysis using mass spectrometry. The study confirmed that the Company's novel anti-sense oligonucleotides 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^[1].

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. HCC is the fourth-leading cause of cancer mortality worldwide and accounts for ~90% of liver cancers^[2] with an estimated market size of \$8 billion (7% CAGR)^[3]. Elevated Midkine has been associated with progression, metastasis and chemotherapy resistance in liver cancer^[4] and because of the limited efficacy of conventional therapy^[5], the 5-year survival rate is just 21% (American Cancer Society)^[6].

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

Scientia Associate Professor Orazio Vittorio, Head of Immune Oncology Lab, UNSW, commented:

"As researchers in cancer biology, our recent experiments have unveiled a promising breakthrough in liver cancer treatment. Through the utilization of these novel oligonucleotides, we have achieved remarkable in vitro efficacy, successfully inducing a significant reduction in full-length Midkine and generating a non-functional Midkine variant within liver cancer cells. This discovery holds immense potential for patients battling liver cancer, offering a new avenue for therapeutic intervention."

Ajan Reginald, Roquefort Therapeutics, Chief Executive Officer, commented:

"Liver cancer is growing with incidences forecast to increase to one million new patients per year by 2025^[7]. It remains an area of high unmet medical need with a 5-year survival of only 21%^[8] because the existing medicines have limited effect^[9]. Midkine is associated with progression, metastasis and resistance^[10] and we feel this is a cancer in which we should focus our portfolio of Midkine targeting medicines including antibodies, mRNA and the anti-sense oligonucleotides. These oligonucleotides attack a different Midkine region versus the antibodies and mRNA, and this diversity of targeting may be helpful in developing mono or combination therapies.

We are delighted with the progress of the Midkine portfolio through our accelerated development process which was completed on time and in budget. The planned next steps for the oligonucleotide program are in vivo studies, in parallel with our mRNAs in a highly synergistic and efficient set of in vivo studies in Q3-4 2023.

The pre-clinical progress across all our programs is highly encouraging and within budget and in-keeping with our strategy and we look forward to updating shareholders on our pre-clinical and business development progress in due course."

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LEI: 254900P4SISIWOR9RH34

About Roquefort Therapeutics

Roquefort Therapeutics (LSE:ROQ) is a Main Market listed biotech company developing first in class drugs in the high value and high growth oncology segment prior to partnering or selling to big pharma.

Since listing in March 2021, Roquefort Therapeutics has successfully acquired Lyramid Pty Limited, a leader in the development of medicines for a new therapeutic target, Midkine (a human growth factor associated with cancer progression), and most recently acquired Oncogeni Ltd, founded by Nobel Laureate Professor Sir Martin Evans, which has developed two families of innovative cell and RNA oncology medicines.

Roquefort Therapeutics' portfolio consists of five fully funded, novel patent-protected pre-clinical anti-cancer medicines. The highly complementary profile of five best-inclass medicines consists of:

- Midkine antibodies with significant *in vivo* efficacy and toxicology studies;
- Midkine RNA therapeutics with novel anti-cancer gene editing action;
- Midkine mRNA therapeutics with novel anti-cancer approach;
- STAT-6 siRNA therapeutics targeting solid tumours with significant *in vivo* efficacy; and
- MK cell therapy with direct and NK-mediated anti-cancer action

For further information on Roquefort Therapeutics, please visit <u>www.roquefortplc.com</u> and @RoquefortTherap on Twitter.

[2]

https://www.nature.com/articles/s12276-020-00527-1

[3]

https://www.grandviewresearch.com/industry-analysis/liver-cancer-diagnostic-market

[4]

Gowhari Shabgah, A, Ezzatifar, F, Aravindhan, S, et al. Shedding more light on the role of Midkine in hepatocellular carcinoma: New perspectives on diagnosis and therapy. IUBMB Life. 2021; 73: 659- 669. https://doi.org/10.1002/iub.2458

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[6]

https://www.cancer.org/cancer/types/liver-cancer/detection-diagnosis-staging/survival-rates.html

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9;13:1061842. doi: 10.3389/fphar.2022.1061842. PMID: 36569303; PMCID: PMC9780395.

[8]

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[9]

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[10]

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