May 2022

OPTIVA SECURITIES
THE GLOBAL INVESTOR

Roquefort Therapeutics Plc

Midkine-Based Therapies for Cancer, Chronic Inflamation, Autoimmune Disorders & Covid-19

OPTIVA SECURITIES
THE GLOBAL INVESTOR

Dan Ingram	Research Analyst	+44 (0) 203 137 1902
Robert Emmet, FCA	Corporate Broking	+44 (0) 203 981 4173
Ben Maitland, CFA UK Society	Corporate Finance	+44 (0) 203 034 2707
Graeme Dickson	Dealing Desk	+44 (0) 203 411 1880
Mike Garnet	Dealing Desk	+44 (0) 203 981 4191
Christian Dennis, CEO	Corporate Broking	+44 (0) 203 137 1903

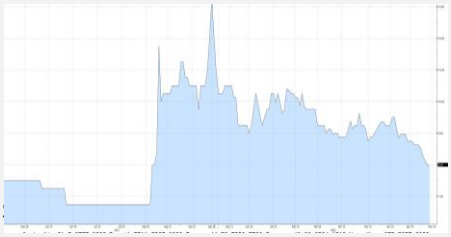
Roquefort Therapeutics plc*

17 May 2022

Company Details

Share Price (Mid):	8.56p**
12month High / Low	**6.75p-13.25p**
Target Price (Fully Diluted)	**19.9p (+132.5%)**
Ticker:	ROQ.LSE
Reporting Currency	GBP
LSE Sector:	Biotech
Key Market Data	
Market:	London Stock Exchange (LSE)
No. Shares in Issue (m)	71.9m
No. Shares Fully Diluted (m)	106.9m
Market Capitalisation	GBP 5.9m
Net Debt (Cash)	GBP (2.49)m
Other EV Adjustments	None
Enterprise Value (EV)	**GBP 3.41m**
Next Results (Interims)	Q4 2022
Year end	31 December

1-Year Share Price Chart



Company Objective: **Growth**

Roquefort Therapeutics is a LSE Main Market listed biotech company developing products through the pre-clinical phase prior to partnering or selling to big pharma. The Company is focused on developing first in class Midkine inhibiting RNA therapeutic drugs for the treatment of cancer, chronic inflammatory, autoimmune disorder and COVID-19. Recent progress within RNA therapeutics has led to a reduction in drug development timelines and costs, increasing the chance of early value creation.

***Optiva Securities acts as Broker to Roquefort Therapeutics plc.**

**Share price correct at 8am on 17/05/22

Patents filed pave the way for rapid progress…

Roquefort Therapeutics plc (ROQ.LSE) ("Roquefort" or the "Company"), is a London listed biotech company focused on early-stage opportunities in the biotechnology & therapeutics sector. In particular, the Company is focused on developing first-in-class Midkine inhibiting RNA therapeutic drugs for the treatment of cancer, chronic inflammatory and autoimmune disorders, as well as lung diseases such as COVID-19. Midkine is a protein found in the body, which when overexpressed has been linked to a wide array of cancers and other diseases. Through its 100% owned subsidiary LYRAMID Pty Ltd, acquired in December 2021 for a £1m cash and shares consideration, Roquefort holds the largest single portfolio of patents and research into Midkine inhibition worldwide. To date over AU$40m has been invested into the intellectual property now held by Roquefort. Most recently, the Company has further strengthened their board with the appointments of Jean Duvall and Dr Simon Sinclair, together adding almost 50 years of pharmaceutical and MedTech experience to Roquefort's already exemplary leadership team.

- **Composition of Matter patent filed:** On March 21, Roquefort announced that it had filed its first composition of matter patent application, covering antisense oligonucleotide drugs to block the action of Midkine in the body. This patent aims to protect the IP and the significant potential value of this new class of RNA therapeutic drug. Provisional composition of matter patents act as an umbrella patent, providing broad IP protection for the development of Midkine-based drugs. Subsequent Methods Patents will later be filed to provide more specific IP protections, such as covering the use of the Midkine antisense oligonucleotides in different clinical indications.

- **Multiple Potential Targets**: By virtue of the number of diseases to which Midkine overexpression has been linked, Roquefort has highly diversified opportunities for novel drug development. Midkine inhibition has the potential to revolutionise treatment of cancer, anti-inflammatory & autoimmune diseases, amongst others; markets with a combined value of over $309bn. If Roquefort can show efficacy in the treatment of even one of these diseases, it would be transformational for the Company, and open the door for early exit through a lucrative Big-Pharma sale.

- **Solid Cash Position**: Following the completion of a £3m fundraise in tandem with the Company's RTO acquisition of LYRAMID, Roquefort now has a cash buffer to fund it through its ongoing pre-clinical trials and into its proposed Phase 1b clinical trials in cancer patients. In general, early-stage biotech companies have a high cash burn, so the combination of Roquefort's solid cash position and lean operating style can be considered a less risky proposition compared to market peers.

- **Valuation Summary:** Based on our analysis of market consensus valuation for Roquefort's peers, Optiva have calculated a near term target valuation of £23.30m for the Company. This valuation was calculated using an rNPV assessment over a 2-3 year timeline, which should be more appropriate for the investment horizons of market participants. On a per share basis, this target valuation is equivalent to 32.4p/share using the current issued share capital, or a fully diluted target price of 19.9p/share. Based on current market price of 8.56p/share, this equates to a potential upside of 132.5%.

Important Notice

Investment in this stock is subject to market and other risks. The value of your investment may go down as well as up and you may not get all of your money back. Past performance may be no guide to the future and the opportunities to trade this investment may be infrequent. This research material is a marketing communication and has not been prepared in accordance with legal requirements designed to promote the independence of research and is not subject to any legal prohibition on dealing ahead of dissemination. We do not hold out this research material as an impartial assessment of the values or prospects of the company. Research comment and recommendations have been independently produced by our research department unless otherwise attributed.

Company Background

Roquefort Therapeutics plc

Roquefort Therapeutics, originally incorporated as Roquefort Investments plc, was established as an investment vehicle with a mandate to acquire businesses focused on early stage opportunities in the medical biotechnology sector. Domiciled in the UK, the Company was incorporated in August 2020, and announced admission to trading on the London Stock Exchange's main market in March 2021. The Company raised a total of £1m at IPO, at a price of 5p per share.

Subsequently, Roquefort announced that it had completed an acquisition of 100% of the issued share capital of Lyramid Pty Limited (LYRAMID), an Australian pre-clinical biotech company focused on developing first-in-class Midkine inhibiting RNA therapeutic drugs. The acquisition was agreed for a consideration of £1m, payable in the form of a cash payment of £500k, and the issue 5,000,000 consideration shares at a price of 10p. An additional deferred consideration of shares may be due to LYRAMID depending on certain milestones, as detailed in Appendix 3. An associated RTO fundraise also saw the Company raise £3m in equity funding at a price of 10p per share.

Lyramid Pty Limited

Lyramid Pty Limited, a private biotech company developing Midkine-based drugs, was spun out of ASX -listed biotech company Cellmid Limited (Cellmid) in April 2021. Lyramid, now an Australian domiciled subsidiary of Roquefort Therapeutics plc, has an exclusive global licence to all Midkine related intellectual property owned by Cellmid. The licence has the term of patent life plus five years and cannot be terminated except for material breach. This licence gives LYRAMID access to over 12 years of Midkine research, and the largest patent portfolio of matter and methods patents around Midkine worldwide, into which over AU$40m has been invested since inception.

Midkine was originally discovered in 1988 at Nagoya University, by Professors Takashi Muramatsu and Kenji Kadomatsu. The intellectual property which the professors pioneered at Nagoya was then acquired by the Japanese company Cell Signals in 2001. Cell Signals, funded by venture capital, further developed the Midkine assets and eventually sold these to Cellmid for a consideration of AU$3.5m in 2008. At the time of the sale, Cellmid acquired a large portfolio of method and composition of matter patents covering the use of Midkine and Midkine inhibitors in a range of disease indications. The Company acquired approximately 120 proprietary anti-Midkine antibodies, all of which passed on to LYRAMID following the spin out.

Cellmid's work on Midkine research was broadly split into four clinical areas of application: Cancer, Cardiovascular Disease, Autoimmune Disease, & Kidney Disease . Meaningful insights were gained across all of these fields, however the most progress was made in Cancer research, with the company finding evidence that its Midkine antibodies could function well in terms of slowing primary tumour growth and tumour metastasis during lab and animal testing. Additionally, Cellmid developed a Midkine diagnostic assay (MK ELISA) for assessing Midkine levels in patients as a diagnostic, prognostic and predictive biomarker.

The principle reason why Cellmid chose to spin out LYRAMID was a change in strategic direction for the company. Cellmid management decided that it was in the company's best interest to focus on its existing portfolio of consumer health products, as opposed to drug development, in the process rebranding to Anagenics in 2021. Moreover, drug development programs, especially antibody drugs, are expensive, risky , and time consuming processes, often costing up to $1bn to bring a drug from pre -development to market over a period of 5-10 years. Both Cellmid/Anagenics and LYRAMID maintain strong incentive alignment however, as both would benefit greatly from the commercial success of the licensed Midkine intellectual property.

Valuation

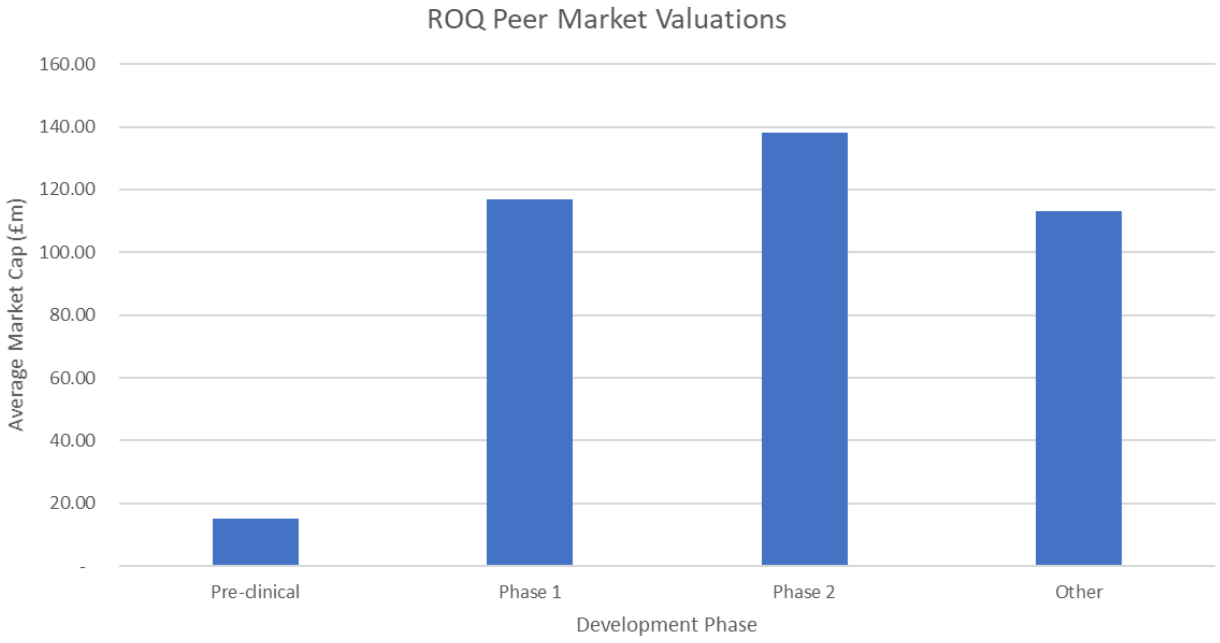
Valuation Summary

As an initiation of coverage for Roquefort Therapeutics, **we ascribe an indicative risked target valuation of £23.30m, equivalent to 19.9p/share on a fully diluted basis.** This valuation uses Roquefort's listed peers as a benchmark for market valuation of biotech development companies during their preclinical and clinical trial stages . The underlying assumption made is a 2 year timeline to Phase 1 Clinical testing (which is slightly pessimistic based on the Company's current schedule). As can be seen from the below graph, the subset of Phase 1 listed peers of Roquefort trade at an average Market Cap of £116.9m, with broadly similar P/B ratios as Roquefort.

rNPV Model. In line with common practice for the valuation of Pharmaceutical companies, we have opted to use an rNPV methodology, both for our near-term and long term valuation assessments. A 12% discount factor has been applied throughout both timelines. We consider this to be a fair discount rate for an early stage, pre-revenue company, and see the potential to relax this assumption somewhat in future revaluations as the Company derisks. Our base case assessment uses a 25% risking factor, a moderately conservative assumption, reflecting the potential risks associated with the transition to Clinical trials.

Upside valuation case based on M&A potential. By nature, early stage biotech companies have a higher risk profile, with the potential for significant upside returns, often through buyouts/ acquisitions, or other accelerated exit strategies. We have also modelled an rNPV for Roquefort based on applicable M&A data, using a 5% risking factor, and outputting a risked valuation of £43m over a 7 year timeline. The model is further detailed in the Pharma Deals/M&A Comparison section of this Note.

Figure 1: ROQ Peer Valuation Averages



Source: Bloomberg

Dilution Factors. Given that Roquefort has a number of outstanding warrants, as well as the deferred consideration shares, we have calculated our per share target price on a fully diluted basis. This equates to effective per share dilution of approximately 62.5% on the basis of a fully diluted share capital of 116,855,000. As the lions share of the warrants exercise around the current market price, we would consider it a reasonable assumption that they be exercised ahead of maturity in a base case forecast. Full issuance of the deferred consideration shares could be considered a more conservative assumption, given their relatively difficult vesting conditions of the market cap respectively reaching £25m and £50m.

Figure 2: Listed Peer Comparison Set

Ticker	Name	Market Cap (£m)	P/B Ratio	Relevant Comparable
STX LN Equity	SHIELD THERAPEUTICS PLC	43.17	0.804	N/A
AGY LN Equity	ALLERGY THERAPEUTICS PLC	167.44	3.044	N/A
ETX LN Equity	E-THERAPEUTICS PLC	128.64	3.898	N/A
TNG FP Equity	TRANSGENE SA	209.11	3.419	Phase 1
BIOV CN Equity	BIOVAXYS TECHNOLOGY CORP	7.59	1.739	Phase 1
COCP US Equity	COCRYSTAL PHARMA INC	39.39	0.666	Phase 1
AUTL US Equity	AUTOLUS THERAPEUTICS PLC	293.91	1.230	Phase 1
ONCR US Equity	ONCORUS INC	34.54	0.348	Phase 1
ADAP US Equity	ADAPTIMMUNE THERAPEUTICS-ADR	254.55	9.696	Phase 2
OCEL US Equity	ORGANICELL REGENERATIVE MEDI	22.02	N/A	Phase 2
BVX LN Equity	BIVICTRIX THERAPEUTICS PLC	15.87	N/A	Pre-clinical
CYTO US Equity	ALTAMIRA THERAPEUTICS LTD	16.38	0.478	Pre-clinical
PHIO US Equity	PHIO PHARMACEUTICALS CORP	9.02	0.539	Pre-clinical
RNAZ US Equity	TRANSCODE THERAPEUTICS INC	27.85	1.577	Pre-clinical
ROQ LN Equity	ROQUEFORT THERAPEUTICS PLC	5.90	1.446	Pre-clinical

Source: Bloomberg

Peer Comparison

Optiva have selected a broad comparable set drawn exclusively from global public equity markets. Peer selection was based on approximate comparability of size, sector, development strategy and similarity of projects (typically drawn from the immunotherapy subsector). Peers were also selected at a variety of development milestones, so as to be able to better estimate relative valuation for Roquefort as it further derisks and enters clinical trials. At time of writing, the average Market Cap of the sample (excluding ROQ) is £90.68m.

Shield Therapeutics PLC (STX LN): Shield Therapeutics plc is a specialty pharmaceutical company focused on the development and commercialization of secondary care-focused pharmaceuticals. The Company's key late-stage products include a novel and effective oral pharmaceutical product for the treatment of iron deficiency anaemia and an iron-based phosphate binder for the treatment of hyperphosphatemia.

Allergy Therapeutics PLC (AGY LN): Allergy Therapeutics PLC is a specialty pharmaceutical company that develops medical drugs for the treatment and prevention of allergies. The Company sells and distributes vaccine products ranging from general seasonal pollen allergy vaccinations for common allergies to patient-specific short run batches for less common allergens.

e-Therapeutics PLC (ETX LN): e-Therapeutics PLC is a systems biology drug discovery company. The Company uses computers to predict the effects of intervention to proteins in a cell. Novel targets can be identified, prioritised and assessed with greater confidence in the biological context. Harnessing internal target gene discoveries, the Company are currently building an in-house pipeline of RNAi-based medicines, using its proprietary GalNAc-siRNA technology.

Transgene S.A (TNG FP): Transgene S.A is a biotechnology company. The Company develops therapeutic vaccines and oncolytic viruses against solid tumours (lung, liver, head & neck and colorectal cancers). In addition to clinical-stage immunotherapies, Transgene S.A. develops individualized therapeutic vaccines and multi-functional oncolytic viruses. The biotech company is focusing its research and development efforts on its therapeutic vaccine and oncolytic virus candidates, which target conditions including breast, lung, prostate, liver, and other cancers. These drug candidates stimulate the immune system to infect and kill cancer cells.

BioVaxys Technology Corp (BIOV CN): BioVaxys Technology Corp. is a clinical-stage biopharma developing antiviral and anticancer vaccine platforms. The Company is evaluating a potential SARS-CoV-2 vaccine based on its haptenized viral protein technology, and advancing a compassionate use trial in the EU to evaluate its haptenized cell vaccine for late-stage ovarian cancer.

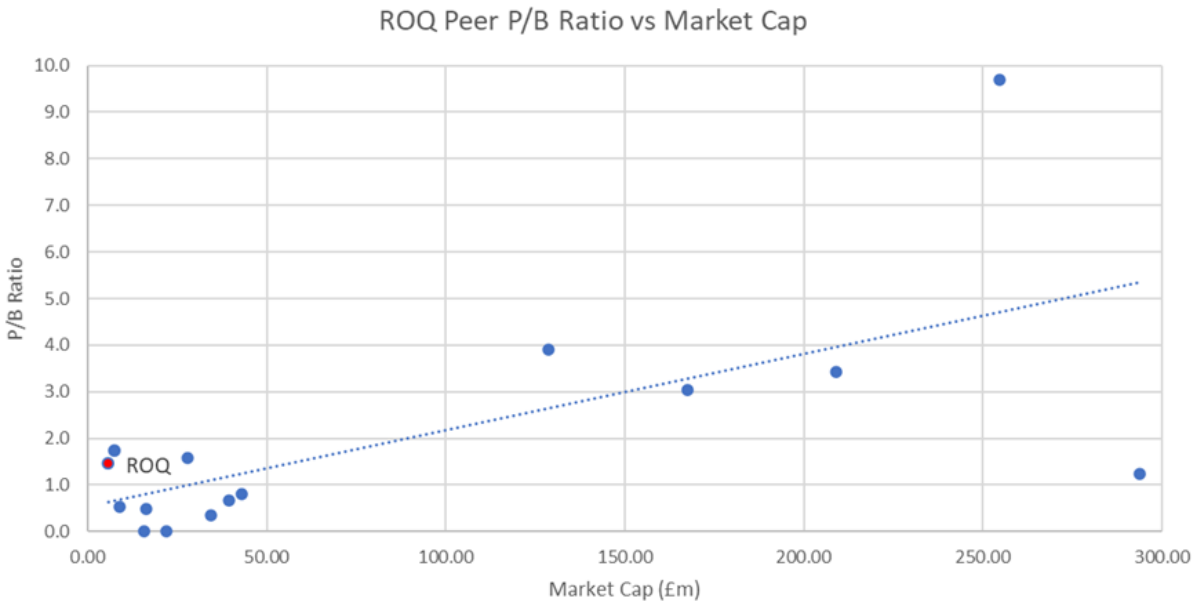
Cocrystal Pharma, Inc (COCP US): Cocrystal Pharma, Inc. operates as a biotechnology company. The Company focuses on developing novel antiviral therapeutics for hepatitis, influenza viruses, and noroviruses. Cocrystal Pharmaare a clinical-stage biotechnology company discovering and developing novel antiviral therapeutics that target the replication process of coronaviruses (including SARS-CoV-2), influenza viruses, noroviruses and hepatitis C viruses. The Company serves patients in the United States.

Autolus Therapeutics plc (AUTL US): Autolus Therapeutics plc is a clinical-stage biopharmaceutical company engaged in the development of next-generation, programmed T cell therapies for the treatment of haematological malignancies and solid tumours. The therapies are designed to help re-programme patients' immune systems to recognise cancer cells more easily. Autolus Therapeutics serves clients in the United Kingdom.

Oncorus, Inc (OCEL US): Oncorus, Inc. operates as a biotechnology company. Oncorus are advancing a pipeline of intratumorally and intravenously administered product candidates for multiple indications with significant unmet need based on our Herpes Simplex Virus (HSV) Platform and our selectively self-amplifying viral RNA (vRNA) Platform. The Company's viral immunotherapies are designed to selectively attack and kill tumour cells and deliver transgenes to stimulate multiple arms of the immune system against tumours. Oncorus serves the healthcare sector in the United States.

Adaptimmune Therapeutics (ADAP US): Adaptimmune Therapeutics is a clinical-stage biopharmaceutical company focused on providing novel cell therapies to people with cancer. It is a leader in the development of T-cell therapies for solid tumours and have seen responses in six different types of solid tumours in clinical trials. Its cell therapy candidates include Specific Peptide Enhanced Affinity Receptor (SPEAR T-cells), which use genetically engineered T-cell receptors; next generation T-cell Infiltrating Lymphocytes (TiLs) where a patient's own T-cells are co-administered with its next generation technology, and HLA-independent TCRs (HiTs) where surface proteins are targeted independently of the peptide-HLA complex. The company is also developing allogeneic or "off-the-shelf" cell therapies utilizing a proprietary allogeneic platform.

Figure 3: Scatterplot of Peer Price-to-Book Ratio against Market Cap (ROQ highlighted in red)



Source: Bloomberg

Organicell Regenerative Medicine, Inc (OCEL US): Organicell Regenerative Medicine, Inc. operates as a biotechnology company. The Company offers research, development, marketing, and manufacturing of new biologic medicine with a focus on current and potential regenerative therapeutics. Organicell Regenerative Medicine serves customers worldwide.

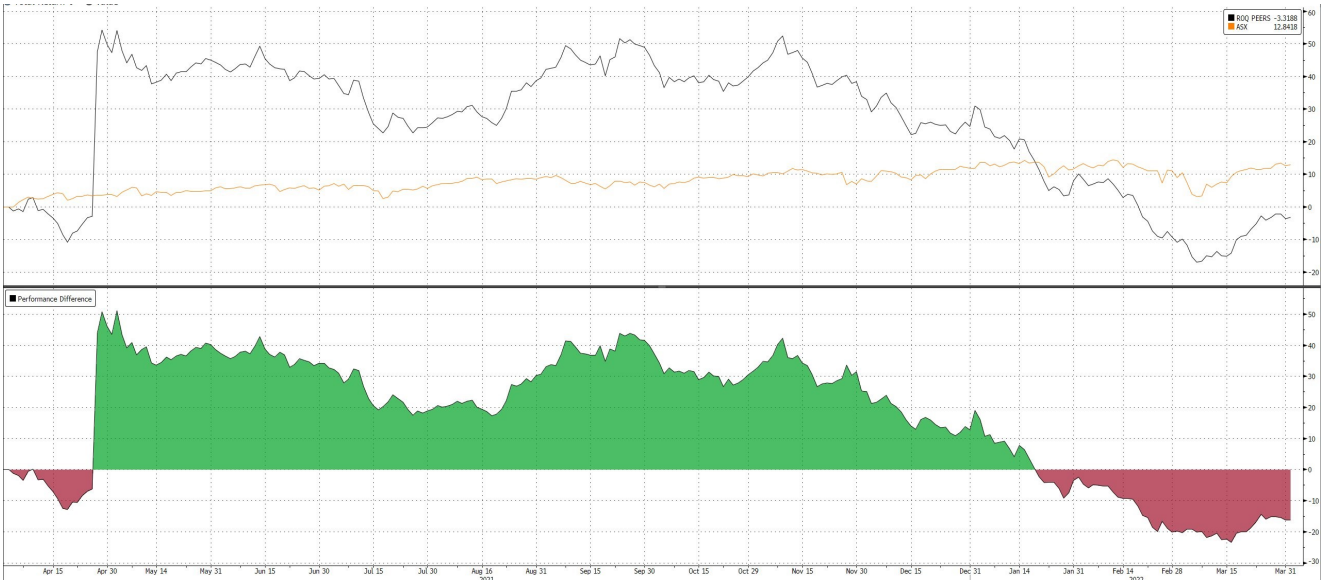
BiVictriX Therapeutics PLC (BVX LN): BiVictriX Therapeutics plc operates as a biotechnology company. BiVictriX is a UK-based drug discovery and development company which is focused on leveraging clinical experience to develop a class of highly selective, next generation cancer therapeutics which exhibit superior potency, whilst eliminating treatment-related toxicities. BiVictriX Therapeutics serves customers worldwide.

Altamira Therapeutics Ltd (CYTO US): Altamira Therapeutics Ltd. operates as a pharmaceutical company. The Company specializes in the development of cochlear therapies for the treatment of acute inner ear tinnitus and acute sensorineural hearing loss from acute acoustic trauma, deafness, and in middle and inner ear surgery. Altamira Therapeutics markets its products worldwide.

Phio Pharmaceuticals Corp (PHIO US): Phio Pharmaceuticals Corp operates as a pharmaceutical company. The Company focuses on cancer immunotherapy, as well as offers medicine for other diseases. Phio is addressing some of the biggest challenges in immuno-oncology (I/O) by developing therapeutics that leverage self-delivering technology to target both tumour and immune cells, enabling efficient RNAi delivery into any cell of interest. Phio Pharmaceuticals serves customers in the United States.

TransCode Therapeutics, Inc (RNAZ US): TransCode Therapeutics, Inc. operates as a biotech company. The Company focuses on developing a proprietary delivery system that has been repurposed to safely deliver optimized therapeutic oligonucleotides to genetic targets in tumours and metastases. TransCode Therapeutics serves customers worldwide.

Figure 4: Relative Performance of an equal weighted basket of ROQ Peers (inc ROQ) against the FTSE All Share over the past 12 months



Source: Bloomberg

Figure 5: M&A Peer Peer Comparison Set

Acquirer/Target	Deal Size ($B)	Upfront ($M)	M&A/License Deal	Applicable Diseases	Stage
J&J/Momenta	6.5	-	M&A	Autoimmune	Phase 2
Gilead/Forty Seven	4.9	-	M&A	Cancer	Phase 1b
Merck/VelosBio	2.8	-	M&A	Cancer	Phase 2
Amgen/Five Prime	1.9	-	M&A	Cancer	Phase 2
Boehringer Ingelheim/ NBE	1.4	-	M&A	Cancer	Phase 1
NJCCTQ/Abpro	4.0	60	License	Cancer immuno-oncology	Discovery
Gilead/Nurix	2.4	45	License	Cancer & immune	Preclinical
Novo-Nordisk/ Corvidia	2.1	725	License	CKD Cardio-renal, Chronic inflammation	Phase 2b
Mallinckrodt/Silence	2.1	25	License	Diversified	Preclinical/Phase 1
Genentech/Skyhawk	2.0	undisclosed	License	Cancer, Autoimmune, Neurodegenerative	Discovery/ Preclinical
Alexion/Zealand	2.0	40	License	Diversified	Discovery

Source: Company

Pharma Deals/M&A Comparison

The above table shows a sample of major Pharmaceutical company transactions executed between 2019-2021 in adjacent fields to Roquefort's ongoing Research & Development. In particular, the green highlighted transactions (Mallinckrodt/Silence & Genentech/Skyhawk) have been deemed by management as being particularly appropriate comparables, based on a combination of development stage and their being early stage oligonucleotide/mRNA based drug programs.

Using these transactions as a foundation, we have prepared an upside case rNPV valuation based on the implicit assumption of Roquefort achieving a transaction exit as opposed to carry a development project to market. An average deal size has been calculated from the above sample, with the highlighted transactions given quadruple weight based on their particular comparability, giving an average transaction value of $2.61bn.

As with our base case valuation, a 12% discount rate has been used, with the same justifications. A much longer timeframe has been assumed, with the pay-out discounted over a 7 year leadup. This assumption is designed to be conservative, given that it is already assessing a blue-sky potential outcome, however based on the above table it can be seen that transactions can occur far earlier. Note of course that Roquefort intends to be commencing Phase 1 trials as early as 2023.

A risk factor of 5% has been applied to the unrisked NPV of $1.18bn, reflecting the myriad of risk vectors between an early stage company such as Roquefort and such an exit. Again, more optimistic views could be taken as to the upside potential of a buyout for Roquefort, but such transactions are infrequent relative to the number of players in the market.

Overall, this model outputs a risked valuation of £43.01m as a potential 'M&A Valuation' for Roquefort, equivalent to 36.8p per share on a fully diluted basis. This model arguably reflects the value potential of holding ROQ for a longer term, however for many investors a 7+ year investment horizon may not align with investment goals.

Midkine:

Background

Midkine is a heparin-binding protein which is a growth factor involved in many diseases. While barely detectable in healthy adults, Midkine is overexpressed in conjunction with cancer, inflammatory conditions and autoimmune disorders. The protein is known to be prominent in embryogenesis, but has been observed to have a role in preventing tumour cell death, as well as promoting metastatic spread to other organs, tumour angiogenesis, cell growth, and resistance to chemotherapy, thereby contributing to various levels of cancer progression and reduced patient survival. Midkine also contributes to lung pathology in Acute Respiratory Disease Syndrome (ARDS), ventilation induced lung injury, sepsis, pulmonary arterial hypertension and fibrosis. Additionally, elevated levels of Midkine have been observed in hospitalized COVID-19 patients.

Midkine was discovered in 1988 at Nagoya University in Japan by Professors Muramatsu and Kadomatsu. Since its discovery, Midkine and its role in many disease processes has been the subject of over 1,000 scientific publications. A series of papers demonstrated that Midkine contributes to kidney, chronic cardiac, lung and liver diseases; autoimmune disorders; osteoporotic fracture healing; neural injury and neurodegenerative disorders. In oncology, elevated Midkine is a biomarker for all solid and haematological cancers examined thus far. Effectively, Midkine hinders the normal immune response to tumours, and reduces the efficacy of cancer immunotherapy treatments. In particular, Midkine causes resistance to immune checkpoint inhibitors in cancer patients.

First approved for use in advanced melanoma treatment in 2011, checkpoint inhibitors were the most significant paradigm shift in the treatment of cancer in a generation. These novel cancer immunotherapies allowed the patient's own immune system to be harnessed to attack the tumour cells. However, they don't work for every patient with many only gaining minimal or no benefit in terms of recurrence and long-term survival. Around 50% of melanoma patients do not respond to ICIs, while up to 90% of patients with other tumours do not gain any benefit. Roquefort believes there is strong evidence that Midkine inhibition represents a viable approach to the immunotherapy resistance problem.

Figure 6: Roquefort Therapeutics Midkine Program proposed milestones

2021	2022				2023		
Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3
Collaboration for MK-oligonucleotide design and testing	Phosphoro-diamidate Morpholin-Oligonucleotide (PMO) drug production	MK-AO drug delivery vehicle design & testing	MK-AO + delivery vehicle medium scale manufacture		Scalable Good Manufacturing Practice (GMP) production	Investigational New Drug (IND) enabling studies	Investigational New Drug (IND) application
In vitro optimisation and screening	Lead MK-AO candidate selection	Cancer cell in vitro efficacy testing	Mouse tumour experiments	Mouse tumour experiments – cancer immunotherapy	Pharmacokinetic/Toxicity/ Biodistribution studies Cancer Immunotherapy experiments In vivo Inflammatory & autoimmunity experiments		Clinical trial preparation
	Composition of Matter Provisional Patent 1	Composition of Matter Provisional Patent 2	Methods Patent 1	Methods Patent 2		Methods Patent 3	Patent Cooperation Treaty (PCT) International Filing

Source: Company

Cancer Immunotherapy

Melanoma was where the early checkpoint inhibitor drugs were first investigated because skin cancer has traditionally been the archetypical tumour for understanding tumour immune responses, and melanoma was long known to be amenable to immunotherapy. Investigation into the mechanisms by which melanoma can metastasise through the body via the lymphatic system found that Midkine, which has long been known to be elevated in cancer, induced the formation of new lymphatic vessels that, in turn, act as the conduit to spread the tumour to other parts of the body. Furthermore, Midkine secreted by melanomas can help create a tumour immune microenvironment that enables the melanoma to evade the immune system. Specifically, Midkine influences macrophages to become tolerant to the cancer so that the immune system cannot generate the T cells that would normally kill cancer cells.

Given the known role of Midkine in the metastasis and spread of cancer, combined with the extremely large potential market for supplementary drugs which improve efficacy of checkpoint inhibitors, this represents an ideal development target for Roquefort. Midkine is highly expressed in around 30 malignant tumour types but is almost absent in healthy people. It also makes for an excellent cancer biomarker, as it is present at the initial stages of cancer development, informing both diagnosis and potential treatment response. Various studies have suggested that Midkine antibodies could be more specific and sensitive for biomarkers present in cancer than other, better-known biomarkers.

The current addressable market for cancer immunotherapy drugs stands at approximately $75bn, representing around 50% of all oncology drugs. Whilst it is hard to assess the potential market share Roquefort could achieve from this, given that Midkine inhibition would work in tandem with existing drugs as opposed to replacing them, it is evident that increasing the efficacy of such a large drug market would be massively lucrative.

COVID-19

Research studies have also shown that Midkine is involved in various lung diseases and multi-organ failure, as well as impacting on a key molecule required for entry of SARS-CoV-2 virus into lung cells. Therefore, Roquefort believe that targeting Midkine may be beneficial for preventing SARS-CoV-2 infection and the devastating symptoms of acute and long COVID-19.

As with cancer treatment, once Roquefort have developed a safe and effective way to inhibit Midkine production by the body, they will be in a position to commence in vitro testing for their efficacy in inhibiting COVID-19 infection as well as in vivo pre-clinical trials of COVID-19 disease progression. Whilst such treatments are arguably 'late to the party', as COVID cases become less severe and vaccine rollouts continue, testing will provide valuable insight into the effect of Midkine inhibition on SARS variants in general, including the prospect of using such inhibitors to treat novel COVID variants.

The current global COVID therapeutics market stands at approximately $14.6bn, and is forecast to almost double to $25.6bn by 2030, in particular as the world assesses the threat of rapidly mutating COVID variants with the potential to trigger another global pandemic. Beyond simply being a massive addressable market, research into potential COVID treatments still maintains both prestige and newsworthiness, potentially raising the profile of a growth company such as Roquefort.

Chronic inflammatory diseases and Autoimmune disorders

As previously detailed, Midkine's role in an array of disease progressions is well documented, with conditions ranging from Rheumatoid Arthritis, Multiple Sclerosis, Kidney inflammation, Chronic inflammatory heart failure, lung and liver diseases; autoimmune disorders; osteoporotic fracture healing; neural injury and neurodegenerative disorders showing demonstrable Midkine contribution. Whilst these are not necessarily the immediate core focus of Roquefort, the breadth of applicable fields for testing Midkine inhibitors effectively acts as diversification for the Company. Whilst many pharmaceutical and therapeutics companies have a very narrow focus, meaning that setbacks or underwhelming lab results can entirely halt projects, Roquefort has the luxury of being able to pivot direction should a particular avenue of research prove fruitless.

Combined, the global markets for Anti-Inflammatory and Autoimmune treatment drugs total over $200bn, more than double that of cancer immunotherapy. Over 4% of the world's population is affected by some form of Autoimmune disease, meaning that it is relatively safe to assume that whatever field Roquefort can achieve a combination of safety and efficacy of treatment in, there will be an extremely large addressable market.

Risk Factors

Funding Risk. Novel drug development is known to be an expensive process, requiring multiple rounds of funding to derisk projects with no guarantee of return on investment. Whilst Roquefort is presently in a strong cash position, and is fully funded to achieve its near term goals, the Company will need to continually raise further funds as it progresses through clinical trials, regulatory approvals and eventually market penetration. Inability to raise sufficient funds could slow, hinder or even entirely halt the Company's growth trajectory.

Regulatory Risk. Pharmaceutical companies are subject to some of the most stringent regulation of any industry, particularly with regard to the development of novel drugs and therapeutics. Key regulatory focus areas are safety and efficacy, and future clinical trials conducted by Roquefort may be suspended or abandoned entirely in the event that regulatory agencies consider that continuation of these trials could expose participants to undue risks, regardless of whether said trials can demonstrate efficacy.

Development Risk. As with any Research & Development project, results are not guaranteed with biotech development. Whilst initial results have shown highly promising data for the use of Midkine-based drugs across a variety of diseases, there is no guarantee that these results will prove to be significant under more rigorous testing particularly when applied directly to human patients. Furthermore, even if Midkine is effectively targeted, this may not result in sufficient improvement in therapeutic outcomes in humans to deliver commercial success for a drug of this nature.

Competition Risk. As a whole, the biotech sector is a complex and fast-moving industry, with an array of institutions and organisations taking a variety of approaches to disease treatment and prevention. Rapid scientific and technological change within the biotech sector could lead to other market participants creating approaches, products and services equivalent or superior to the diagnostic testing products and services than those to be offered by Roquefort. Additionally, the Company will need to constantly maintain and protect its IP across multiple jurisdictions. It is possible that competitors will use similar technologies in jurisdictions where the Enlarged Group has not registered patents.

Appendix 1: Forecast Accounts

Roquefort Therapeutics, Summary Financials			
Fiscal Year To: December	**Dec-2021A**	**Dec-2022E**	**Dec-2023E**
All figures in Constant Currency			
Income Statement (£ 000's)			
Revenue	1	0	0
Other Income	0	0	0
Total Growth (%)	*N/A*	*N/A*	*N/A*
Total Income	**1**	**0**	**0**
Cost of Goods Sold	10	0	0
Gross Profit	**-9**	**0**	**0**
Gross Margin (%)	*N/A*	*N/A*	*N/A*
SG&A	-252	-900	-902
Transaction Costs	-407	-106	0
Share Based Payments to Management	-248	0	0
R&D Expenditure	-1	-340	-590
% Sales	*N/A*	*N/A*	*N/A*
Reported Operating Profit (EBIT)	-917	-1,346	-1,492
Cash Flow Adjustments;	0	0	0
Adjusted EBITDA	**-917**	**-1,346**	**-1,492**
Adj. EBITDA Margin (%)	*N/A*	*N/A*	*N/A*
Net Interest paid	0	0	0
Reported PBT	-917	-1,346	-1,492
Effective Tax Rate (%)	*N/A*	*N/A*	*N/A*
Adjusted Earnings	**-917**	**-1,346**	**-1,492**
Dividend Distribution	0	0	0
Reported Total Comprehensive Profit (Loss)	-917	-1,346	-1,492
Attributable to:			
Roquefort Shareholders	-917	-1,346	-1,492
Non-Controlling Interest	0	0	0
	-917	-1,346	-1,492
Weighted Av. NOS (millions)	**71.9**	**71.9**	**71.9**
Fully Diluted, WA NOS(millions)	106.9	106.9	106.9
Adjusted EPS (GBp)	**-1.28**	**-1.87**	**-2.08**
Adjusted, Diluted EPS (GBp)	-0.86	-1.26	-1.40

Appendix 1: Forecast Accounts

Cash Flow Statement (£ 000's)			
Reported Operating Profit	-917	-1,346	-1,492
Depr & Amortisation	0	0	0
WC Movements *	-1,992	2,106	7
Share Based Payments	367	0	0
Tax Paid / Other	-81	247	331
Cash Flow from Operations (CFFO)	**-2,623**	**1,007**	**-1,154**
Tangible & Intangible Capex	1,106	0	0
Def Cons Payment / Other	0	0	0
Cash Flow from Investing (CFFI)	**1,106**	**0**	**0**
Net Equity Issuance	4,630	0	0
Net Interest (paid) /received, plus fees	0	0	0
Dividends Paid	0	0	0
Debt Issuance (Paydown), Net	0	0	0
Other / Adj	40	0	0
Cash Flow from Financing (CFFF)	**4,670**	**0**	**0**
Opening Cash Position	0	900	1,907
Cashflow	3,153	1,007	-1,154
FX, Other	1	1	0
Closing Gross Cash Position	900	1,907	753
Closing Gross Debt Position	0	0	0
Closing Net Debt (Cash)	**-900**	**-1,907**	**-753**
Balance Sheet (£ 000's)			
Intangible Assets	1,016	1,016	1,016
Tangible Assets	133	133	133
Other LT Assets	0	0	0
Current Assets (Ex Cash)	2,136	30	30
Gross Cash & Equivalents	858	1,907	753
Total Assets	**4,142**	**3,086**	**1,932**
Current Liabilities, ex ST Debt	128	135	142
Short Term Debt	0	0	0
Long Term Debt	0	0	0
Other Long Term Liabilities	0	0	0
Total Liabilities	**128**	**135**	**142**
Net Assets	**4,014**	**2,951**	**1,790**
Attributable Capital & reserves	4,014	2,951	1,790
Non-Controlling Interests	0	0	0
Total Equity & Reserves	**4,014**	**2,951**	**1,790**
Basic NOS (Period end, millions)	71.9	71.9	71.9

Appendix 2: Management Profiles

- **Stephen West: Executive Chairman**

  Stephen West holds a Bachelor of Commerce and is a Fellow Chartered Accountant with over 26 years of financial and corporate experience gained in public practice, oil and gas, mining, and investment banking. Mr West has a proven track record in working with growth companies with extensive experience in IPOs, secondary listings, corporate finance, fundraisings, investor relations and financial and management reporting. Mr West is currently non-executive chairman and co-founder of Zeta Petroleum plc and non-executive director of EnergyPathways Limited. Mr West previously held senior positions in several listed companies including AIM listed Tomco Energy Plc where he was Chairman from February 2020 to October 2020, ASX listed Apollo Consolidated Limited where he was a Non-Executive Director from 2012 to 2018, and Oslo listed PetroNor E&P Limited where he was Executive Director and Chief Financial Officer until February 2020.

- **Dr Graham Robertson: Chief Scientific Officer**

  Graham Robertson gained his PhD in molecular virology from Macquarie University, Australia before undertaking Post-Doctoral training in gene regulation and nuclear architecture at Oxford. He returned to Australia as a Post-Doc in the laboratory of Prof. Emma Whitelaw at University of Sydney where he set up a transgenic mouse facility and discovered repeat-induced silencing as an epigenetic process on mammalian transgenes. Dr Robertson then moved to Westmead Hospital Millennium Institute where he pursued studies on the fibrotic liver disease NASH and the impact of inducible xenobiotic/drug interactions on drug clearance pathways. A component of this work involved creating a transgenic mouse model for studying gene regulation of human CYP3A4, the main pathway for drug metabolism. The model was subsequently commercially leveraged as a screening tool for drug development. At the ANZAC and Garvan Institutes in Sydney (2004-2014), Dr Robertson explored the impact of cancer-associated inflammation in repressing drug clearance leading to excessive toxicity. Dr Robertson also explored the link between chronic inflammation and disrupted energy metabolism as the basis for cancer cachexia. A key discovery from this work was the activation of thermogenesis in white & brown fat, linked to body wasting. These findings were published in Cancer Research and Cell Metabolism where it was ranked amongst the 10th highest papers in the latter journal. He has published ~60 papers with >3,000 citations.

- **Professor Trevor Jones: Strategic & Scientific Advisor**

  Professor Trevor Jones CBE FMedSci has had a distinguished career in the pharmaceutical and biotech industry spanning over 45 years, having previously been main Board Director for Research & Development at The Wellcome Foundation (Wellcome plc), where he was responsible for the development of a number of significant products across several therapeutic areas attracting reimbursement, as well as OTC formulations. Prof. Jones also served as a Non-Executive Director of Allergan Inc from 2004 to 2015 during which time the company made a number of key acquisitions. During Prof. Jones career, he has served on the Boards of a number of other private and publicly listed companies and industry bodies across the UK, USA and Europe. In particular, he was a former Director General of the Association of the British Pharmaceutical Industry where he directed all the activities related to UK pharmaceutical industry government relations on behalf of national and international pharmaceutical companies.

- **Dr Michael Stein: Non-Executive Director**

  Michael Stein is a business leader and strategic adviser with C-suite experience in healthcare. Dr Stein was the founding CEO of Valo Therapeutics and also of OxStem Ltd, a biotechnology spin-out from the University of Oxford. In addition, Dr Stein has served as founding CEO for Doctor Care Anywhere, acquired by Synergix in 2015. In 2001, he co-founded the Map of Medicine Ltd (the Map) with University College London. As founding CEO (and later CMO), the Map was nationally licensed across NHS England (2005-15) and acquired by Hearst Business Media (HBM) in 2008, after which Dr Stein transitioned to executive vice-president of healthcare innovation. Dr Stein graduated as a medical doctor (Honours) and biochemist (First Class Honours) from the University of Cape Town (1988) and from the University of Oxford (Rhodes Scholar) with a doctorate in Physiological Sciences (Immunology). He subsequently was appointed as a Junior Research Fellow in Medicine at Trinity College, Oxford (1992-95) having been a part-time lecturer in Immunology and Pathology at Balliol College, Oxford (1988-91).

Appendix 2: Management Profiles

- **Jean Duvall: Non-Executive Director**

  Jean Duvall is a highly accomplished individual 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 US$700 million to US$2 billion in revenue. During her time at Ferring, Jean led or co-led over 10 transactions and had legal oversight on over 25 transactions. Jean has a significant track record in corporate development having led multiple successful M&A, divestment and licensing deals throughout her career. 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. Trizell in particular received several multi-billion dollar offers for its lead oncology gene therapy product, Adstiladrin, which is now in the registration phase. Jean is currently CEO and Co-Founder of ReproNovo, a women's health and reproductive medicine company focussing on R&D and manufacturing with potential products entering phase 2 and phase 1.

- **Mark Freeman: Non-Executive Director**

  Mark Freeman is a Chartered Accountant and has more than 25 years' experience in corporate finance and the listed markets with a focus on project development. Mr Freeman is a graduate of the University of Western Australia with a Bachelor of Commerce with a double major in Banking & Finance and Accounting as well as holding a Graduate Diploma in Applied Finance with a major in Investment Analysis from the Securities Institute of Australia. He has experience in strategic planning, business development, acquisitions and mergers, project commercialisation, and project development and general management. Prior and current experience with Panoramic Resources Ltd, Calima Energy, Digital BTC, and Pursuit Minerals Ltd.

- **Dr Simon Sinclair: Non-Executive Director**

  Dr Sinclair is a commercial physician scientist leader with 20 years' pharma, medtech and consumer healthcare industry experience in translational medicine, clinical development, medical affairs, evidence-based market access, medical safety, vigilance and real-world evidence in both executive and non-executive roles. During his career, Simon has held senior roles at Johnson and Johnson and Merck & Co. Simon is currently Chief Safety Officer of Reckitt Benckiser Group plc ("Reckitt") where he is responsible for guiding and evaluating the safety of all its products to protect its consumers, and for building and maintaining consumers' trust in Reckitt. Additionally, Simon is a Non-Executive Board member of Ondine Biomedical Inc., an AIM listed life sciences company focused on photodisinfection-based therapies to prevent and treat a broad spectrum of infections, including those caused by drug-resistant pathogens. He is also Non-Executive Director at Renovos Biologics Limited, an orthopaedic biotech company. Simon is a renowned scientist with a PhD in neural transplantation from Cambridge University, medical degree and numerous publications in scientific journals throughout his career.

- **Maria Halasz : Strategic Adviser**

  Maria Halasz has been involved with biotechnology companies for over 27 years and is the former CEO of Lyramid, having been working with Lyramid since its inception, and is the former Chief Executive and Managing Director of Anagenics Ltd (formerly Cellmid Ltd). Ms Halasz initially worked in executive positions in biotechnology firms, then managed investment funds and later held senior positions in corporate finance specialising in life sciences. An accomplished public company CEO with international experience, Ms Halasz has executed transactions in the US, China, Europe, Japan and the UK. Maria is a graduate of the University of Western Australia (B.Sc., MBA) and the Australian Institute of Company Directors (GAICD). She has board experience in public and private companies and has acted on advisory boards of non-profit organizations. A passionate innovator, Ms Halasz is inventor of several patents and co-author of peer reviewed publications.

Appendix 3: Ownership Structure

Shares in Issue

At time of writing, Roquefort has an issued share capital of 71.9m shares. 51% of these shares were in issue prior to the RTO, 42% were issued as placing shares in relation to the transaction, and the balancing 7% were issued as Consideration Shares to acquire LYRAMID. The Company has a Free Float of 57.65%, being shares held outside of Concert Parties or holders in excess of 3% ownership.

Figure 7: Capital Structure

	Number of Shares
Shares	
Current Shares in Issue (excluding LYRAMID Consideration)	66,900,000
LYRAMID Consideration	5,000,000
Total Issued Share Capital	**71,900,000**
Deferred Consideration Shares	10,000,000
Total Warrants	34,955,000
Fully Diluted Share Capital	**116,855,000**

Source: Bloomberg, Company

Figure 8: Disclosable Stakeholders

Stakeholder	Number	Percentage Holding
J Whiddon	7,300,000	10.15%
A Lachab	7,200,000	10.01%
Provelmare Holdings S.A *(The previous beneficiary owner of LYRAMID)*	5,000,000	6.95%
S West	4,550,000	6.33%
M Rollins	4,000,000	5.56%
S Marr	2,400,000	3.34%
Free Float	41,450,000	57.65%

Source: Bloomberg, Company

Outstanding Warrants

Roquefort has a total of 34.96m warrants outstanding, the majority of which issued in conjunction with the Company's two placings. 28.96m of these warrants are held by various investors and Advisors, all exercising at a price of 10p per share. Additionally, there are a total of 6m Directors Warrants in issue, exercising at an average price of 13.13p across 3 tranches.

Deferred Consideration Shares

Pursuant to the acquisition of LYRAMID, the Company agreed that deferred consideration shares should be issued to the vendor under the following conditions:

- if prior to the fifth anniversary of Admission, the Company's market capitalisation exceeds £25,000,000 for a period of 5 or more consecutive trading days the Company shall issue to the Seller (or its nominee) 5,000,000 Ordinary Shares; and
- if prior to the fifth anniversary of Admission the Company's market capitalisation exceeds £50,000,000 for a period of 5 or more consecutive trading days the Company shall issue to the Seller (or its nominee) a further 5,000,000 Ordinary Shares.

OPTIVA SECURITIES
THE GLOBAL INVESTOR

THIS DOCUMENT IS NOT FOR DISTRIBUTION INTO THE UNITED STATES, JAPAN, CANADA OR AUSTRALIA

General disclaimers

Investment in this stock is subject to market and other risks. The value of your investment may go down as well as up and you may not get all of your money back. Past performance may be no guide to the future and the opportunities to trade this investment may be infrequent. This research material is a marketing communication and has not been prepared in accordance with legal requirements designed to promote the independence of research and is not subject to any legal prohibition on dealing ahead of dissemination. We do not hold out this research material as an impartial assessment of the values or prospects of the company. Research comment and recommendations have been independently produced by our research department unless otherwise attributed.

This is a marketing communication under the rules of the Financial Conduct Authority ("FCA"). It has not been prepared in accordance with legal requirements designed to promote the independence of investment research and is not subject to any prohibition on dealing ahead of the dissemination of investment research.

This document, which presents the Optiva Securities Limited ("OSL") research department's view, cannot be regarded as "investment research" in accordance with the FCA definition. The contents are based upon sources of information believed to be reliable but no warranty or representation, expressed or implied, is given as to their accuracy or completeness. Any opinion reflects OSL's judgement at the date of publication and neither OSL, nor any of its affiliated or associated companies, nor any of their directors or employees accepts any responsibility in respect of the information or recommendations contained herein which, moreover, are subject to change without notice. OSL accepts no liability whatsoever (in negligence or otherwise) for any loss howsoever arising from any use of this document or its contents or otherwise arising in connection with this document (except in respect of willful default and to the extent that any such liability cannot be excluded by the applicable law).

This document is confidential and is being supplied solely for your information. It must not be copied or re-distributed to another person / organization without OSL's prior written consent.

This is not a personal recommendation, offer, or a solicitation, to buy or sell any investment referred to in this document. The material is general information intended for recipients who understand the risks associated with investment. It does not take account of whether an investment, course of action, or associated risks are suitable for the recipient.

OSL manages its conflicts in accordance with its conflict management policy. For example, OSL may provide services (including corporate finance advice) where the flow of information is restricted by a Chinese wall. Accordingly, information may be available to OSL that is not reflected in this document. OSL and its affiliated or associated companies may have acted upon or used research recommendations before they have been published.

This document is approved and issued by OSL for publication only to UK persons who are authorized persons under the Financial Services and Markets Act 2000 and to professional clients, as defined by Directive 2004/39/EC as set out in the rules of the Financial Conduct Authority. Retail clients (as defined by rules of the FCA) must not rely on this document.

Specific disclaimers

OSL acts as Broker to Roquefort Therapeutics plc (ROQ) and OSL's private and institutional clients hold shares in ROQ. Opinions and estimates in this document are entirely those of OSL as part of its internal research activity. OSL has no authority whatsoever to make any representation or warranty on behalf of ROQ.

NEITHER THIS DOCUMENT NOR ANY COPY OF IT MAY BE TAKEN OR TRANSMITTED INTO THE UNITED STATES OF AMERICA, OR DISTRIBUTED, DIRECTLY OR INDIRECTLY, IN THE UNITED STATES OF AMERICA OR TO ANY US PERSON AS DEFINED IN REGULATION S UNDER THE UNITED STATES SECURITIES ACT OF 1933. ANY FAILURE TO COMPLY WITH THIS RESTRICTION MAY CONSTITUTE A VIOLATION OF UNITED STATES SECURITIES LAWS.

NEITHER THIS DOCUMENT NOR ANY COPY OF IT MAY BE TAKEN OR TRANSMITTED INTO CANADA OR DISTRIBUTED IN CANADA OR TO ANY INDIVIDUAL OUTSIDE CANADA WHO IS A RESIDENT OF CANADA, EXCEPT IN COMPLIANCE WITH APPLICABLE CANADIAN SECURITIES LAWS.

NEITHER THIS DOCUMENT NOR ANY COPY OF IT MAY BE TAKEN OR TRANSMITTED INTO AUSTRALIA OR DISTRIBUTED IN AUSTRALIA OR TO ANY RESIDENT THEREOF EXCEPT IN COMPLIANCE WITH APPLICABLE AUSTRALIAN SECURITIES LAWS. ANY FAILURE TO COMPLY WITH THIS RESTRICTION MAY CONSTITUTE A VIOLATION OF AUSTRALIAN SECURITIES LAWS.

NEITHER THIS DOCUMENT NOR ANY COPY OF IT MAY BE TAKEN OR TRANSMITTED INTO OR DISTRIBUTED INTO JAPAN OR TO ANY RESIDENT THEREOF FOR THE PURPOSE OF SOLICITATION OR SUBSCRIPTION OR OFFER FOR SALE OF ANY SECURITIES. ANY FAILURE TO COMPLY WITH THIS RESTRICTION MAY CONSTITUTE A VIOLATION OF JAPANESE SECURITIES LAWS.

NEITHER THIS REPORT NOR ANY COPY HEREOF MAY BE DISTRIBUTED IN ANY JURISDICTION OUTSIDE THE UK WHERE ITS DISTRIBUTION MAY BE RESTRICTED BY LAW. PERSONS WHO RECEIVE THIS REPORT SHOULD MAKE THEMSELVES AWARE OF AND ADHERE TO ANY SUCH RESTRICTIONS.

Copyright © 2021 Optiva Securities Limited, all rights reserved. Additional information is available upon request.

Optiva Securities Limited, 49 Berkeley Square, Mayfair, London, W1J 5AZ
Tel: 0203 137 1902, Fax: 0870 130 1571
Member of the London Stock Exchange. Authorized and regulated by the Financial Conduct Authority.