Roquefort Therapeutics PLC

Programme update

6 November 2023

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Significant Mesodermal killer cell therapy milestone

Roquefort Therapeutics today announced that its Mesodermal killer (MK) cell program has reached a significant milestone. The Company's MK cells are a proprietary and novel class of cellular medicine, capable of killing cancer cells directly and priming / activating natural killer (NK) cells. The combination of this direct killing of cancer cells and activation of NK cells to increase cytotoxicity have each been demonstrated in validated *in vivo* models of lymphoma and myeloma.

In the results announced today, MK cells were tested in combination with NK cells. The activation of NK cells produced up to a two-fold increase in cytotoxicity over NK cells alone in three different difficult to treat cancers: Ovarian cancer (P<0.01); Acute myeloid leukaemia (P<0.05); and Multiple myeloma (P<0.01). The Company's MK cells will now progress into further in vivo studies in validated models of NK cell activation and cancer cytotoxicity.

Commercial potential: This demonstration of the activation of NK cells in multiple cancer types including solid tumours, lymphomas and leukaemia is a significant commercial milestone because the NK cell activation is a highly attractive modality for large pharmaceutical companies. The recent transactions in this promising market include the $1.4bn partnership between Sanofi and Innate Pharma announced in December 2022 and >$300m Gilead and Dragonfly Therapeutics transaction in May 2022 for Dragonfly's proprietary activators of NK cells.

Growth potential of NK cell therapeutics market: The global NK cell therapeutics market is at a nascent stage and there is no approved NK cell therapy yet in the market. According to forecasts by Research and Markets in 2022, the global NK cell therapeutics market is expected to grow from $297m in 2024 to $5.676bn in 2032 at a CAGR of 44.59%, driven by the rising number of clinical trials and the increasing incidence and prevalence of cancer cases.

Hybridan's view: Kuick Research in March 2023 indicated that there are more than 200 NK cell therapies under clinical trials. We believe Roquefort's MK cell program is unique in composition of matter and methods, attractive to pharma companies or private equity firms not yet involved in this space, and synergic to other approaches under development to harnessing the innate benefits of NK cells or the wider immunity system. Hence, we think some details about recent industry transactions in NK cell therapeutics help to set the scene for investors in anticipation of the commercial potential of Roquefort's MK cell program.

Key Statistics:

Code	ROQ
Listing	LSE; OTCQB
Sector	Biopharma
Market cap*	£8.7m
Shares in issue*	129.15m
Current price*	6.75p
12-month high/low*	9p/6p
Free float**	55%

**Closing price on 3 November 2023. High/low based on closing prices. **Free float based on Hybridan estimates.*

Share Price Performance

Year to date	2%
Past 12 months	-5%
2022	-37%

Source: Alpha Terminal

Financials Y/E Dec (£)

Item	Annual Dec-21	Annual Dec-22	Interim Jun-23
Sales	719	-	200,000
EBT	(917,433)	(1,634,303)	(937,436)
Cash	899,721	2,322,974	1,379,021

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 natural-killer-mediated anti-cancer action; and (5) siRNA targeting novel STAT-6 target in solid tumours.

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Roquefort's Mesodermal killer (MK) cell program

MK cells are a novel engineered cell type to kill cancer directly, attract NK cells and to activate (prime) natural killer cells to kill cancer. MK cells were derived from the novel cellular medicine platform invented by Nobel Laureate, Prof. Sir Martin Evans' team. Prof. Sir Martin Evans, the 2007 Nobel Laureate in Physiology or Medicine, is currently Roquefort's Executive Director and Group Chief Scientific Officer.

Roquefort's MK cells are patented and identified by a unique 'finger print' consisting of seven unusual receptors detectable on the surface of the MK cells (CD16, CD96, CD112, CD137L, CD178, CD253 and CD277) and the absence of three more common cell surface markers (CD34, CD45 and CD56). The seven receptors present on MKs confer key functions in direct cytotoxicity cells via contact-dependent cell lysis (destruction) or antibody-dependent cell-mediated cytotoxicity (ADCC) and through the attraction and priming of NK cells.

A key advantage of the MK cells is that they are mesodermal cells, which are typically safe. There is good evidence that these mesodermal cells are safe in human subjects. Thus, MK cells are cytotoxic, but are not expected to induce any of the side effects of other cytotoxic cellular therapies, such as Chimeric Antigen Receptor-T (CAR-T) cells. In particular, MK cells are not expected to induce cytokine release syndrome (CRS; aka cytokine storm), macrophage activation syndrome (MAS) and off-target effects.

Industry transactions in NK cell activation

NK cells are lymphocytes in the same family as T and B cells, coming from a common progenitor (from which something originates). As cells of the innate immune system, NK cells respond quickly to a wide variety of pathological challenges. NK cells exhibit unparalleled cytotoxic activities against cells not regarded as 'self.' To carry out its cytotoxic activity, NK cells contain granzymes and perforins which cause the target cell to lyse, in other words break apart into smaller pieces. Perforin is a pore-forming protein and also known as cytoplasmic granule toxins. Granzyme is a family of structurally related serine proteases stored within the cytotoxic granules of cytotoxic lymphocytes. Perforin and granzyme induce target-cell apoptosis or death cooperatively, in other words acting together.

Innate Pharma: ANKET (Antibody-based NK cell Engager Therapeutics) platform

Innate Pharma's technology is based on a new class of molecules, built with fragments of monoclonal antibodies, to induce synthetic immunity against cancer by providing proliferation and activation signals targeted to NK cells.

Sanofi is Innate Pharma's long-term partner for NK cell therapeutic development. The two companies first partnered in 2016 to develop two bispecific NK cell engagers. This initial partnership, valued at more than $460m, focused on activating the NKp46 receptor, which is expressed on all natural killer cells. The first asset from this partnership, SAR44379, is in Phase I/II studies for multiple forms of leukaemia. SAR44379 is an NKp46/CD16-based CD123-targeted NK cell engager developed with the ANKET platform.

In December 2022, Sanofi and Innate Pharma SA announced an expansion of their collaboration, with Sanofi licensing IPH62 targeting B7-H3 and with the option to add up to two additional ANKET targets. The deal size is $1.4bn, including upfront, milestones and potential royalties on future sales.

It is worth noting that Sanofi paid approximately US$359m in November 2020 to acquire Kiadis Pharma for its allogeneic NK cell technology platform; engineered lymphokines that stimulate NK cells.

Dragonfly Therapeutics: TriNKET (tri-specific NK engagers) platform

TriNKETs is a multi-specific immune engager technology that seeks to recruit NK cells as the innate immunity and cytotoxic T cells as the adaptive immunity to fight cancer in the tumour microenvironment. Bristol Myers Squibb (BMS), Merck & Co., AbbVie and Gilead are among the TriNKET licensees.

BMS and Dragonfly Therapeutics began their collaboration in 2017 focusing on haematology malignancies. To date, BMS has licensed in multiple candidates from the TriNKET program.

Merck & Co. began its collaboration with Dragonfly Therapeutics in 2018, initially focusing on a number of solid tumour targets and with a deal size value at $695m for several solid-tumour programs from the TriNKET technology platform.

In May 2022, Gilead announced a $300m upfront payment to Dragonfly for DF7001, a preclinical candidate that targets 5T4+ expressing cells, including tumour cells, cancer-associated fibroblasts and cancer stem cells. In addition, Dragonfly is eligible to receive potential opt-in payments and performance-based development, regulatory and commercial milestone payments, as well as royalties of up to 20% on worldwide net sales.

Financial Statements

Income Statement (£) Y/E December	Annual 2021	Annual 2022	Interim 1H22	Interim 1H23
Revenue	719	-	-	200,000
Other income	130	-	-	-
Cost of goods	(10,069)	-	-	200,000
Administrative expenses	(252,392)	(1,306,561)	(485,530)	(765,611)
Costs associated with the IPO	(182,053)	-	-	
Share based payments	(248,326)	(8,427)	(57,511)	(5,201)
Costs associated with acquisition	(224,744)	-		
Research and development expenditure	(698)	(319,315)	(69,288)	(365,435)
Amortisation of Intangible assets	-	-	(149,952)	-
Depreciation	-	-	-	(1,189)
Operating loss	(917,433)	(1,634,303)	(762,281)	(937,436)
Finance income	-	-	-	-
Profit (loss) before tax	(917,433)	(1,634,303)	(762,281)	(937,436)
Taxation	-	18,886	-	155,078
Profit (loss) for the period	(917,433)	(1,615,417)	(762,281)	(782,358)
Other comprehensive loss	624	(14,989)	-	39,525
Total comprehensive income (loss)	(916,809)	(1,630,406)	(762,281)	(742,833)
Earnings (loss) per share	(3.71)	(1.56)	(2.05)	(0.64)
Weighted average number of shares	24,701,793	103,479,476	37,209,663	121,850,000

Balance Sheet (£) Y/E December	Annual 2021	Annual 2022	Interim 1H22	Interim 1H23
Property, Plant & Equipment	-	-	-	52,855
Intangible assets	1,481,530	5,343,505	1,331,578	5,343,505
TOTAL NON-CURRENT ASSETS	1,481,530	5,343,505	1,331,578	5,396,360
Trade and other receivables	2,178,783	101,738	98,520	345,832
Cash and cash equivalents	899,721	2,322,974	3,328,573	1,379,021
TOTAL CURRENT ASSETS	3,078,504	2,424,712	3,427,093	1,724,853
TOTAL ASSETS	4,560,034	7,768,217	4,758,671	7,121,213
Deferred tax liabilities	281,911	281,911	281,911	281,911
TOTAL NON-CURRENT LIABILITIES	281,911	281,911	281,911	281,911
Trade and other payables	195,517	279,670	1,094,389	370,298
TOTAL CURRENT LIABILITIES	195,517	279,670	1,094,389	370,298
TOTAL LIABILITIES	477,428	561,581	1,376,300	652,209
Share capital	719,000	1,291,500	719,000	1,291,500
Share premium	3,460,595	4,403,094	3,460,595	3,460,595
Share based payments reserve	366,708	375,135	424,219	380,336
Merger relief reserve	450,000	3,700,000	450,000	3,700,000
Retained deficit	(914,321)	(2,548,728)	(1,676,602)	(3,331,086)
Currency translation reserve	624	(14,365)	5,159	25,160
TOTAL EQUITY	4,082,606	7,206,636	3,382,371	6,469,004
TOTAL LIABILITIES AND EQUITY	4,560,034	7,768,217	4,758,671	7,121,213

Source: Company Data

Cash Flow Statement (£) Y/E December	Annual 2021	Annual 2022	Interim 1H22	Interim 1H23
Profit (loss) before tax	(996,068)	(1,634,303)	(762,281)	(937,436)
Adjustment for:				
Foreign exchange	765	(9,918)	(5,160)	31,865
Non-cash adjustment	(2,602)	-	-	-
Depreciation	-	-	-	1,189
Share based payment	366,708	8,427	57,511	5,201
Taxation	-	18,886	-	-
Changes in working capital:				
Change in trade and other receivables	(24,434)	(20,318)	2,083,286	(86,268)
Change in trade and other payables	129,525	59,750	(121,325)	96,922
Change in inventory	9,273	-	-	-
CASHFLOWS FROM OPERATING ACTIVITIES	(516,833)	(1,577,476)	1,401,983	(888,527)
Purchase of property, plant & equipment	-	-	-	(54,043)
Acquisition of subsidiary, net of cash acquired	(606,226)	(103,478)	-	-
CASHFLOWS FROM INVESTING ACTIVITIES	(606,226)	(103,478)	-	(54,043)
Proceeds from issue of ordinary shares	2,182,798	3,121,202	1,015,000	-
Share issuance costs	(159,405)	(18,990)	-	-
CASHFLOWS FROM FINANCING ACTIVITIES	2,023,393	3,102,212	1,015,000	-
Net change in cash & cash equivalents	900,335	1,421,258	2,416,983	(942,570)
FX translation difference	(614)	1,995	11,869	(1,383)
Cash at the beginning of the period	-	899,721	899,721	2,322,974
Cash at the end of the period	899,721	2,322,974	3,328,573	1,379,021

Source: Company Data

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