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Pharmaceuticals & Biotechnology

Source: Eikon Thomson Reuters

Market data	
EPIC/TKR	VAL
Price (p)	6.05
12m High (p)	7.73
12m Low (p)	0.90
Shares (m)	263.41
Mkt Cap (£m)	15.94
EV (£m)	16.23
Free Float*	92%
Market	AIM

**As defined by AIM Rule 26*

Description

ValiRx is a clinical-stage biopharmaceutical company focused on novel treatments for cancer and associated biomarkers. It currently has two products in Phase I/II and Phase II clinical trials. Its business model focuses on out-licensing or partnering drug candidates after clinical trials

Company information	
CEO	Dr Satu Vainikka
CFO	Gerry Desler
Chairman	Oliver de Giorgio-Miller
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	www.valirx.com

Key shareholders	
Directors	0.6%
Yorkville	4.9%
Nicholas Slater	2.7%

Diary	
21 Dec 2017	General Meeting
1Q-18	Read-out VAL201
1Q-18	Full read-out VAL401

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ValiRx

Clinical efficacy of VAL401

ValiRx is a clinical-stage biopharmaceutical company focused on the development of therapeutics for the treatment of cancer, associated biomarkers and companion diagnostics. The company's two leading assets are in clinical trials: VAL201 (Phase I/II) – a peptide for advanced prostate cancer and potentially other hormone-induced indications; and VAL401 (Phase II) – a reformulation of risperidone, in trials for lung cancer. Early clinical analysis of its Phase II trial with VAL 401 has been released, meeting its primary endpoint by providing a statistically significant improvement in the overall survival rate. Further data will be revealed in due course.

- **Strategy:** ValiRx operates as a virtual business, out-sourcing most of its activities. The core strategy is to develop its therapeutic assets through the clinical pathway and seek a partner/licensing deal to complete the development programme and regulatory submissions to commercialise the products.

- **Overall survival data:** The newly published data on non-small cell lung cancer patients that exhausted all possible existing therapies, provide statistically significant improvement in the overall survival rate. Further analyses in quality of life and characterising the best responders will be revealed in due course.

- **Valuation:** This data provides an important value inflection point which was not reflected previously in the share price. The market has reacted promptly to this news, with the share price jumping from 1p at the end of November (capital increase) to 7.73p – a near eight-fold increase!

- **Next steps:** Safety and tolerability of VAL401 has been confirmed in late stage patients affected by non-small cell lung cancer. The study has provided also the dosing level that will be used in subsequent trials. Full data analysis is underway, and the final read-out of the study is expected in the near future.

- **Investment summary:** The market has failed to recognise the potential of ValiRx, fretting more about the need for more capital to advance its clinical programmes that taking a rational view of the likely success of its clinical candidates. Given the clinical progress seen to date, the company will be attracting the attention of potential commercial partners and/or institutional investors in order to achieve the true value of its assets.

Financial summary and valuation

Year end Dec (£000)	2014	2015	2016	2017E	2018E	2019E
Sales	88	83	0	0	0	0
SG&A	-1,514	-1,645	-1,666	-1,750	-1,837	-1,929
R&D	-1,772	-1,543	-2,375	-2,850	-3,421	-4,105
EBITDA	-2,958	-2,877	-3,939	-4,502	-5,155	-5,936
Underlying EBIT	-2,958	-2,888	-3,949	-4,508	-5,165	-5,941
Reported EBIT	-3,138	-3,029	-3,987	-4,734	-5,399	-6,182
Underlying PBT	-2,952	-2,889	-5,531	-4,581	-5,195	-5,995
Statutory PBT	-3,641	-2,567	-5,569	-4,807	-5,429	-6,235
Underlying EPS (p)	-10.5	-7.7	-8.2	-2.6	-1.3	-1.4
Statutory EPS (p)	-13.5	-6.7	-8.2	-2.8	-1.3	-1.5
Net (debt)/cash	453	232	-734	559	-4,194	-9,588
Capital increases	2,510	2,681	2,615	3,964	0	0

Source: Hardman & Co Life Sciences Research

Overall Survival data

At the end of September, ValiRx provided the market with the first set of data from its Phase II trial with VAL401 in advanced non-small cell lung cancer (NSCLC) patients. This has now been followed by early data demonstrating the benefit of VAL401 on overall survival in these patients.

Part I: Pharmacokinetic data

Previously reported pharmacodynamic data are in line with the traditional formulation of risperidone

The pharmacokinetic data represented an important step in ValiRx's development plan for VAL401. Being able to show that the drug was well absorbed and metabolised following a therapeutically active dose, and consistent with those seen with the traditional tablet formulation.

- VAL401 was readily absorbed, as evidenced by the presence of the active ingredient and its primary metabolite in the bloodstream. Analysis revealed also the predicted difference in absorption and metabolism of VAL401 compared with documented outcomes using conventionally formulated risperidone
- Blood levels of risperidone and its metabolite in patients taking VAL401 were consistent with those seen with comparable doses in pre-clinical investigations
- Safety and tolerability profile of 2mg of VAL401 in this patient population was also acceptable, which will be the dosing regimen used in subsequent trials.

Part II: Clinical evidence

- Eligibility for the Phase II trial were patients with stage IV NSCLC that had failed on prior chemotherapy with 3-6 months life expectancy, and classified as having adenocarcinoma as a subset of the lung cancer
- There were no other therapeutic options for these patients other than palliative care
- Eight patients were recruited into the trial and seven have been used for the Overall Survival analysis (there was uncertainty about the date of first treatment in one patient who was therefore disregarded for survival analysis)
- Each patient was acclimatised onto the drug regimen on an escalation dose starting at 2mg per day, until they reached either 10mg per day or their maximum tolerated dose if lower
- Benchmark patients (19 untreated): patients that would have been eligible for the trial but for a reason did not participated
- Data were collected and analysed by Ariana, an independent clinical research organisation

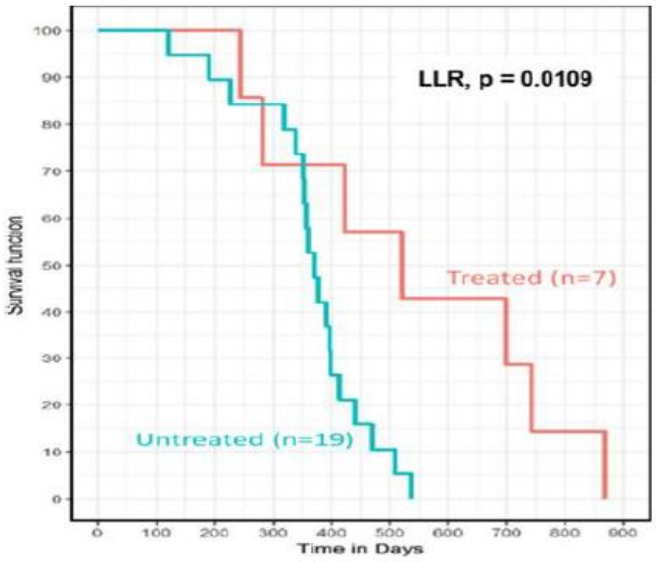
Overall Survival data

VAL401 meets its primary endpoint of providing efficacy in extending the life expectancy of NSCLC patients

Overall survival is defined by the National Cancer Institute as "*The length of time from either the date of diagnosis or the start of treatment for a disease, such as cancer, that patients diagnosed with the disease are still alive. In a clinical trial, measuring the overall survival is one way to see how well a new treatment works*".

The following Kaplan-Meier graph represents the impact of VAL401 on these late stage patients. It is compared to a group of 19 similar patients that did not receive VAL401.The starting point is the date of first chemotherapy treatment. This outcome represents an important value inflection point for the company.

Kaplan-Meier overall survival



Kaplan-Meier Survival Graph showing length of time in days of patient Overall Survival from time of first lung cancer chemotherapy treatment as a proxy for date of diagnosis

Source: ValiRx

VAL401 confers a statistically significant extension to life expectancy in late stage NSCLC patients

Despite the trial being on a very small patient population, there was a clear distinction between patients treated with VAL401 and those that received only palliative care. Time zero (t=0) corresponds to the start of chemotherapy. Even though the population was a group of very sick patients, there is a clear distinction in overall survival of those treated with VAL401, which was statistically significant to the survival in the group of patients that did not receive treatment. The statistical outcome had not been expected in such a small patient population.

VAL401 as an anti-cancer agent

VAL401 is a proprietary formulation of risperidone

ValiRx, within subsidiary ValiSeek, is developing VAL401, which is a new formulation of risperidone (Risperdal, Johnson & Johnson), originally developed for the treatment of schizophrenia. In contrast to the conventional tablet formulation of risperidone, VAL401 is a liquid lipid-filled capsule containing risperidone plus rumenic acid (a conjugated naturally occurring linoleic acid).

The specific formulation of VAL401 allows the inhibition of the mitochondrial enzyme HSD10...

... which has a protective effect against fast growing cancer cells.

The anti-cancer activity is only present in the specific and proprietary formulation of VAL401, due to an alteration of the lipophilicity of the complex, allowing cellular absorption, given that no anti-cancer activity is found when risperidone or rumenic acid are administered alone. VAL401 is thought to inhibit a mitochondrial enzyme called hydroxysteroid dehydrogenase type 10 (HSD10) that is a crucial component in the maintenance of cellular homeostasis in healthy cells. The complex formation of risperidone and rumenic acid allows the drug to enter the cancerous cell, a characteristic that is not possible with risperidone alone. This mechanism enables VAL401 to target the HSD10 protein and thereby disrupt cancer energy metabolism, breaking the cancer cell cycle.

What to expect next

- Patient Quality of Life data
- Further analysis of the pharmacokinetic data
- Characterising the best responders using Ariana's proprietary KEM artificial intelligence technology for future trial enrolments and patient selection
- A proposed Phase III trial in ca.200 late-stage NSCLC patients with and without standard of care

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(Disclaimer Version 3 – Effective from May 2017)

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