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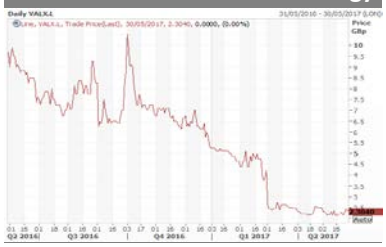
Pharmaceuticals & Biotechnology



Source: Eikon Thomson Reuters

Market data	
EPIC/TKR	VAL
Price (p)	2.30
12m High (p)	17.30
12m Low (p)	2.06
Shares (m)	133.36
Mkt Cap (£m)	3.07
EV (£m)	3.80
Free Float*	97%
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
	+44 20 3008 4416
	www.valirx.com

Key shareholders	
Directors	1.4%
Yorkville	1.8%

Diary	
4Q-17	Read-out VAL201, VAL401
Nov-17	Interims

Analysts	
Martin Hall	020 7194 7632
	mh@hardmanandco.com
Dorothea Hill	020 7194 7626
	dmh@hardmanandco.com
Gregoire Pave	020 7194 7628
	gp@hardmanandco.com

ValiRx

Developing novel cancer therapies

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 potential to treat other hormone-induced indications; and VAL401 (Phase II) – a novel reformulation of risperidone, in trials for lung cancer. Both drugs are targeted at multi-billion dollar markets that are inadequately served by current drugs. The aim is to progress the clinical data and exit via a collaboration or commercial out-licensing to a larger partner.

- **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.
- **Assets:** ValiRx has two novel products (VAL201, VAL401) in clinical development for which evidence of their respective advantages is expected in 2017. VAL301 is in late pre-clinical development for endometriosis, together with VAL101, an interesting a gene silencing platform. VAL has global rights to related biomarkers.
- **Valuation:** Whether by DCF or peer group comparisons, ValiRx is undervalued by the market. A basic DCF on VAL201 and VAL401 only, using modest pricing and market penetration assumptions, generates a risk-adjusted NPV of £31.8m (10.4x current market cap). The discrepancy using peer analysis is even greater.
- **Risks:** New and/or first-in-class drugs carry the risk that they might fail in clinical trials. However, the substantial safety history of the active ingredient in VAL401 and the consistent safety record to date in the VAL201 trial mitigate these risks. More capital is needed to further its proprietary assets along the value chain.
- **Investment summary:** ValiRx is undervalued. The reason for this is certainly its need for more capital to advance its clinical programmes, thereby building value. Given the clinical progress seen to date, the company should be attracting potential commercial partners and/or institutional investors in order to achieve the real 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	-4,622	-5,292	-6,092
Statutory PBT	-3,641	-2,567	-5,569	-4,848	-5,525	-6,332
Underlying EPS (p)	-10.5	-7.7	-8.2	-3.4	-3.3	-3.8
Statutory EPS (p)	-13.5	-6.7	-8.2	-3.6	-3.5	-3.9
Net (debt)/cash	453	232	-734	-3,224	-8,073	-13,564
Capital increases	2,510	2,681	2,615	1,090	0	0

Source: Hardman & Co Life Sciences Research

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Executive summary

Background

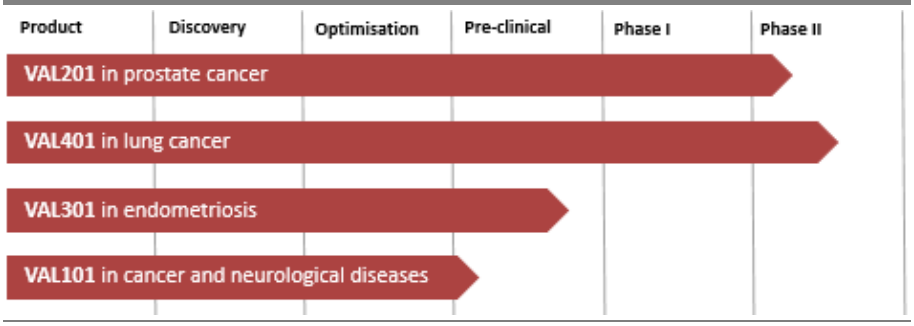
ValiRx is a clinical stage development company with a focus on finding novel treatments in oncology

ValiRx was founded in September 2006 following a reverse takeover with Azure Holding plc. Since the company has acquired assets through a series of transactions and collaborations with prestigious partners such as Imperial College London and Cancer Research UK. Today, ValiRx is a clinical stage drug development company with a focus on the discovery and development of novel treatments in oncology. ValiRx adopts a virtual business model, outsourcing all of its pre-clinical and clinical development work. Through a series of Placings and Convertible Loans, ValiRx has raised ca.£23m from development since inception to get the company to where it is today.

Pipeline

ValiRx is progressing four products in oncology, with two already in Phase I/II and Phase II clinical development. The portfolio is reasonably diverse in terms of targets, indications, and mechanisms of action, thereby lowering the risk profile.

ValiRx portfolio



Source: ValiRx; Hardman & Co Life Sciences Research

Products in clinical development

ValiRx has two products in clinical trials:
- *VAL201 in advanced prostate cancer*
- *VAL401 in advanced lung cancer*

- **VAL201** is currently in Phase I/II clinical trials for patients affected by hormone-sensitive and hormone-resistant prostate cancer. VAL201 is a peptide that inhibits the interaction between the androgen receptor and/or the oestrogen receptor complex with the Src docking protein. This specific mode of action is shown in pre-clinical studies to provide a potent therapeutic benefit with fewer side effects compared to standard hormone therapy.
- **VAL401** is a reformulated version of the well-known Central Nervous System (CNS) drug, risperidone (Risperdal, JNJ, cumulative sales $44.0bn). This compound is now in a Phase II trial. Its unique and proprietary formulation enables VAL401 to target a key protein (HSD10) in cancer cells, which is involved in cell homeostasis. VAL401 is in a Phase II clinical trial for the treatment of patients with lung cancer.

Products in pre-clinical development

The pipeline also comprises two products currently in pre-clinical evaluation

- **VAL101** is a peptide-oligonucleotide construct targeting the Bcl-2 gene utilising the company's proprietary GeneICE platform. VAL101 enables the selective silencing of a specific gene by mimicking the natural process of the enzymatic deacetylation of histone. Pre-clinical studies have shown potential use in a number of cancer indications.

- **VAL301** is a reformulated version of VAL201, targeting the gynaecological disorder endometriosis, which is a serious health issue among females. VAL301 is currently undergoing further pre-clinical assessment.

Strategy

ValiRx aims to de-risk the drug candidate before licencing out the commercial rights

ValiRx has a clearly defined strategy to develop an early stage pipeline of innovative products focused on oncology, where there is a high unmet medical need. The goal is to provide innovative cancer treatments with potential as 'first-in-class' and/or 'best-in-class' drugs. The strategy is to demonstrate safety and potential efficacy in man before and to continue development with a partner or license-out the commercial rights, thereby substantially increasing the value of the assets.

In November 2015, ValiRx established a US office in Cambridge, Boston, the heart of the biotechnology hub to increase the visibility of ValiRx in the US.

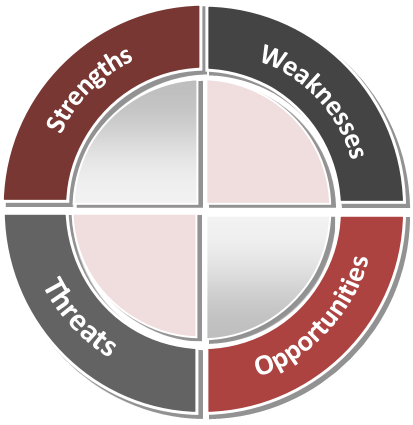
Commercial opportunity

With VAL201 in advanced prostate cancer and VAL401 in advanced lung cancer, ValiRx enters a multi-billion dollar market with high potential and high competition

The two products in clinical trials are both targeting large potential markets which are unsatisfied by current therapies. The need for new drugs to more effectively treat conditions that ValiRx is targeting is abundantly clear. Its approach to prostate cancer is to develop drugs that control hormone induced cancers and abnormal growth either directly or indirectly. Due to the safety profile, there may also be the potential for preventive use. The mechanism of action of VAL201 supports its use in both hormone-dependent and hormone-independent prostate cancer opening it up to a $2-6bn opportunity.

VAL401 is a re-formulation of a well-established CNS drug, risperidone, which has been re-formulated with a naturally occurring plant extract and shown to have activity in improving clinical outcomes of patients with advanced lung cancer. The issue will be the price, which will be benchmarked against the original risperidone. Ultimately this will be decided by ValiRx's eventual commercial partner, but even on a price towards the bottom end of the current range for existing second-line drugs for NSCLC, VAL401 could comfortably reach annual sales in excess of $1,000m p.a.

SWOT analysis



- Two assets in Phase I/II trials
- Proprietary technology
- Re-formulation of a known product
- Concentrates on strengths – outsourcing operations

- Relatively small player in a competitive field
- Clinical trials are capital intensive
- Attrition rates in drug development
- Regulatory risk

- Time & cost of clinical trials
- Competitive field
- Number of technologies and approaches
- Time to conclude licensing deals with pharma majors

- Products with new mechanism of action
- Treatments with opportunities for less side effects
- Target cancers unsatisfied by current therapies
- Endometriosis is very large opportunity

Source: Hardman & Co Life Sciences Research

Newsflow

- VAL201: Completion of dose-escalation phase, followed by dose-expansion phase focusing on dosing schedules.
- VAL401: Phase II trial completion expected end 2017, but amendments of the trial allow earlier data release for pharmacokinetic analysis
- VAL301: Completion of further pre-clinical work throughout 2017

Valuation & investment conclusion

DCF valuation

The combined risk adjusted DCF valuation of VAL201 and VAL401 alone is £31.8m

There is limited information on which to base a comprehensive DCF valuation on the whole company. However, in order to provide readers with a guide, we have undertaken an assessment of ValiRx's clinical-stage assets, VAL201 and VAL401. The risk-adjusted NPV of the royalty streams for VAL201 and VAL401 through to patent expiry are £18.5m and £13.3m respectively. Combining them gives a risk-adjusted NPV of £42.8m, which is 10.4x the current market capitalisation, or 8.4x the current EV. Adding in the other products/technologies would widen this discrepancy.

Peer group comparisons

Analysis of ValiRx relative to a group of UK or international oncology peers (see page 27) also highlights the valuation discrepancy, the relative enterprise value range being 1.8x to 52.9x and 0.2x to 276.5x, respectively. The following table shows the UK comparisons.

UK peer group valuations

Company	Diurnal	Evgen	Sareum	Silence Ther.	Scancell	Tiziana	ValiRx
Ticker	DNL	EVG	SAR	SLN	SCLP	TILS	VAL
Share price	128.5	19.3	0.9	96.0	10.9	203.9	2.30
Shares in issue (m)	52.2	73.3	2,645.2	70.0	261.6	96.2	133.4
Mkt cap (£m)	**67.1**	**14.1**	**23.3**	**67.2**	**28.5**	**196.1**	**3.07**
Cash	30.1	7.1	2.3	39.0	6.5	8.3	0.56
Debt	-3.2	0.0	0.0	0.0	0.0	-13.1	-1.29
EV (£m)	**40.2**	**7.0**	**21.0**	**28.2**	**22.0**	**200.9**	**3.80**
Relative EV	10.6x	1.8x	5.5x	7.4x	5.8x	52.9x	-
Stage of development	Regulatory	Phase II	Phase I/II	Phase II	Phase I/II	Phase I/II	Phase I/II

Prices taken at close of business on 26th May 2017
Source: Hardman & Co Life Sciences Research

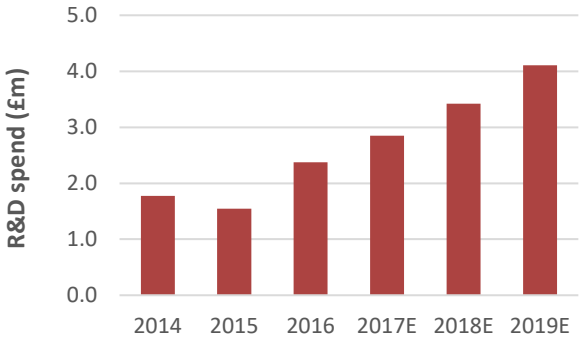
Conclusion

Given that ca.£23m has been invested in R&D to date, there is a clear mismatch between this and the £3.1m capitalisation ascribed to the company by the market. In our opinion, there are two factors affecting this under-rating:

- The company will require more resources to take VAL201 and VAL401 into further development and to promote VAL301 into a Phase I trial for endometriosis
- Apart from the two institutions, Yorkville and Bracknor, that have acquired small shareholdings through conversion of convertible loan notes, ValiRx does not have any institutional shareholders

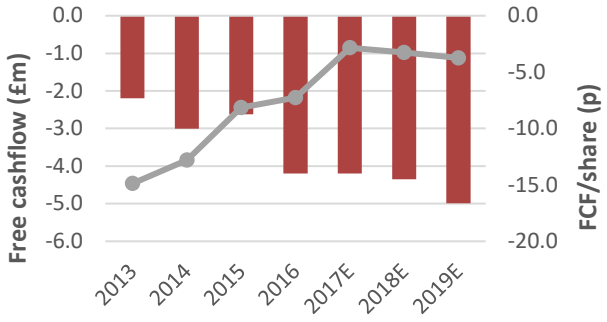
Funding rounds are likely to get larger and ValiRx needs to address its shareholder base at the time of the next capital increase because there is a limit to the support that high net worths (HNWs) can provide. The two institutions that are on the share register recently and currently hold convertible loan notes are present because they see ValiRx as fundamentally undervalued and an outstanding investment opportunity.

R&D investment



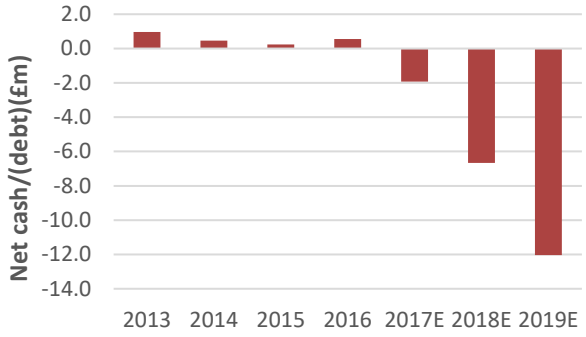
- ValiRx outsources all its research
- Investment is being made to support the two clinical trials (VAL201 and VAL401) with an increase in R&D spends
- R&D cost are expected to increase by ca.£0.5m per year
- Costs have been spread over the expected lifetime of the clinical trials

Free cashflow



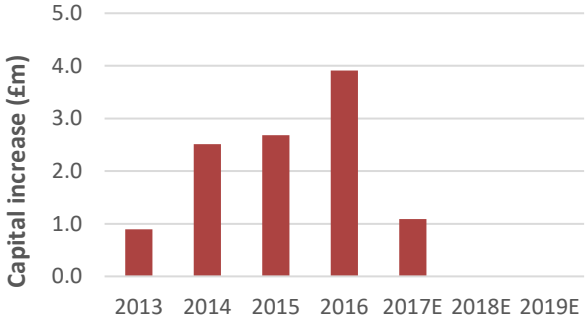
- Cashflow is driven by the corporate overhead (SG&A) and R&D investment
- Offset by the tax credit in R&D investment
- Cash from R&D tax credits is £0.62m in FY16, and expected to rise to £0.7m and £0.9m in FY17 and FY18 as greater investment is made in clinical programmes

Net cash/(debt)



- Net cash at 31st December 2016 was £561k
- A recent capital increase has raised a further £1.2m ross new funds
- Our cash projections suggest that ValiRx will need cash injection later in FY2017 to support the clinical trials
- Annual cash burn of in fiscal 2017 is estimated at ca. £4.2m

Capital increases



- In March 2017, ValiRx raised £1.2m gross (£1.09m net) by way of a Placing.
- Further resources will be needed in the near future

Source: Company data; Hardman & Co Life Sciences Research

ValiRx – the Company

Background

ValiRx is a drug development company…

ValiRx is a clinical stage drug development company with a clear focus on developing novel treatments in oncology and related biomarkers. The goal is to provide innovative treatments with potential 'first-in-class' and/or 'best-in-class' drugs. Since being listed, ValiRx has raised ca.£23m from capital markets to fund development of its pipeline through to early-stage clinical trials. These assets were acquired through a series of licensing deals and collaborations with leading partners such as Cancer Research UK and Imperial College London.

Business model

…that outsources all the pre-clinical and clinical activities

ValiRx has adopted a virtual business model whereby all pre-clinical and clinical development activities are outsourced. This model spreads the risks of life science technology development by minimising financial exposure and running a set of projects to defined commercial end-points. This maximises returns to shareholders relative to the investment made. ValiRx operates through two divisional companies – ValiPharma and ValiSeek.

ValiPharma

ValiRx operates following two operations, ValiPharma and ValiSeek

ValiPharma is the biopharmaceutical arm focused on developing new cancer drugs, currently with three innovative products that can be used potentially in four distinct indications:

- **VAL201** is a peptide currently in Phase I/II trials in prostate cancer
- **VAL301** is a reformulated version of VAL201 for women affected by endometriosis, and is currently in the final stages of pre-clinical assessment
- **VAL101** utilises ValiRx's proprietary GeneICE technology to target the gene expressing the protein Bcl-2, a known cancer target. VAL101 is also in pre-clinical studies

ValiSeek

ValiSeek Limited was formed in 2014 to progress the drug VAL401 through pre-clinical development and Phase II trials for the treatment of lung cancer and other oncology indications. ValiSeek is a joint venture between ValiRx plc (with 60%) and Tangent Reprofiling Limited (40%), which is part of the SEEK Group. The CEO of ValiSeek is Dr Suzanne Dilly, who was instrumental in discovering the anti-cancer activity of VAL401 at SEEK using technology developed at the University of Warwick.

Founded in 2004, SEEK (previously known as PepTcell) is privately-owned. Headquartered in London, SEEK has the goal of bringing safe and low costs medicines to patients as quickly as possible. It does this by:

- Modifying existing drugs to improve efficacy, but keeping existing label, dose and regime costs down
- Drug repositioning, but keeping the dose and dosing regimen the same
- Creating a new medicine in circumstances where no alternatives are available

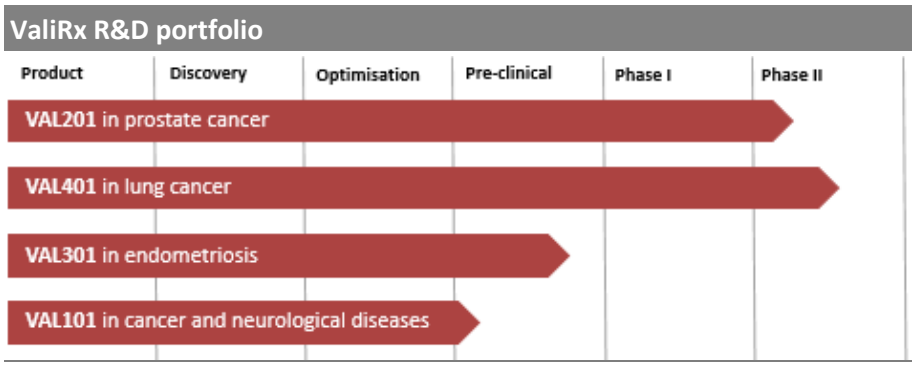
Development portfolio

- Two drugs in clinical trials
- Exciting prospect in pre-clinical development for endometriosis
- Novel proprietary gene silencing platform in pre-clinical evaluation
- Companion biomarkers

R&D pipeline

ValiRx is progressing two projects in clinical development and two projects in pre-clinical study

The vast majority of the ValiRx portfolio is targeted at cancer, but it is diversified in terms of drug classes and products (small molecule, peptide and a gene targeting construct). ValiRx is relatively late-stage, with two products in human trials, and a third drug candidate likely to enter trials in 2018. In parallel, ValiRx is also developing biomarkers to more accurately predict patients in whom its drugs are likely to be effective.



Source: ValiRx, Hardman & Co Life Sciences Research

VAL201

VAL201 is a peptide, with a novel mechanism that inhibits the interaction between the androgen receptor and/or the oestrogen receptor complex and the Src docking protein. It is in Phase I/II trials for hormone-dependent and hormone-independent prostate cancer.

VAL401

VAL401 is a proprietary formulation of risperidone, an established CNS drug. In a formulation with rumenic acid (found in dairy products), the molecule confers anti-cancer activity. VAL401 is currently in Phase II trials for the treatment of advanced non-small cell lung cancer.

Pre-clinical pipeline

VAL301

VAL301 is a proprietary reformulation of VAL201 that is in pre-clinical assessment for the treatment of endometriosis. Trials are expected to commence in 2018 following the completion of further pre-clinical work.

VAL101

VAL101 utilises ValiRx's proprietary gene silencing platform, GeneICE, which prevents the over-expression and/or aberrant expression of genes that promote cell growth. It is presently undergoing late-stage pre-clinical evaluation for halting or reversing tumour growth.

Clinical pipeline

VAL201

- Developed in collaboration with Cancer Research UK
- Phase I/II clinical trials underway in hormone-dependent and hormone-independent prostate cancer
- Entering a poorly-served multi-billion dollar commercial market

Description

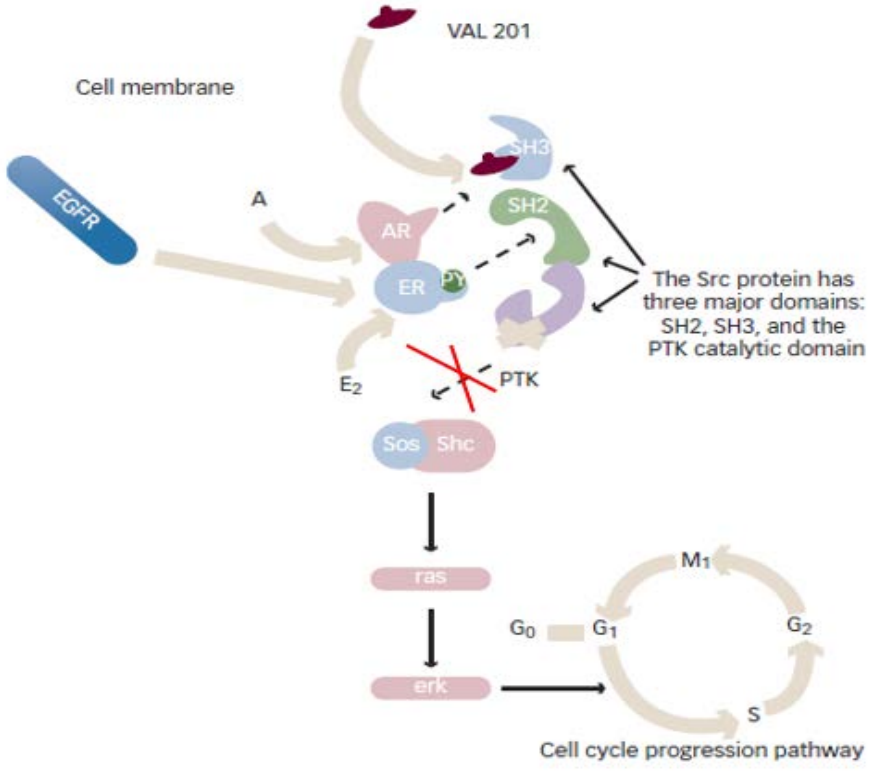
VAL201 comes from a fruitful collaboration with CRUK with potential in hormone resistant and hormone independent prostate cancer

VAL201 has been developed in collaboration with Cancer Research UK (CRUK), with ValiRx owning all the rights, but liable for milestones payments to CRUK. VAL201 is a decapeptide that has potential in treating two types of prostate cancer – hormone-dependent and hormone-independent, and with further potentials for preventive treatment.

VAL201 blocks the interaction between the androgen receptor and/or the oestrogen receptor and the Src kinase, an enzyme known to be involved in many cancers and tumour development through the activation of its signalling pathway. With this mechanism of action, VAL201 would represent a 'first-in-class' therapeutic.

VAL201 has a good pharmacokinetic profile, is stable at ~5°C for 36 months from date of manufacture, and is expected to have a shelf life of over three years.

VAL201 – Mechanism of action

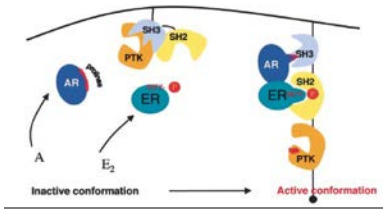


Source: adapted from European Oncology & Haematology, 2012;8(1):32–5

Mechanism of action

In prostate cancer cells, steroid hormones and/or epidermal growth factor trigger the association of the androgen receptor (AR) and/or the oestrogen receptor (ER) complex with Src kinase. This interaction activates the Src protein, causing a cascade of activation, which ultimately stimulates DNA synthesis, cell cycle progression and proliferation.

Src activation



*Source: EMBO, **2000**, Vol19, pp.5406-5417*

VAL201 inhibits Src kinase induced cell proliferation

VAL201 is a protein-protein interaction inhibitor that specifically blocks the interaction of the androgen receptor with Src kinase SH3 domain. The proline-rich peptide mimics a region of the androgen receptor that specifically binds to the SH3 domain of the kinase. By blocking this domain, VAL201 prevents any association between AR and Src and, obstructing the formation of the AR/ER/Src complex. Therefore, VAL201 has the potential to inhibit the signal transduction that leads to cell proliferation. On the other hand, VAL201 does not prevent the association between AR and ER crucial in bone health for example.

Unique mechanism

VAL201 has a unique mechanism of action that enables the inhibition of the Src oncogenic pathway with expected less side effects

Current hormone therapies for advanced prostate cancer are generally untargeted, simply causing androgen deprivation. This subsequently causes undesirable side effects as they block the desired androgen receptor mediated functions in addition to preventing cancer progression. In contrast, because VAL201 is a targeted protein-protein interaction inhibitor that inhibits the specific Src activation cascade, its mechanism offers a completely different approach.

By targeting a specific domain of the Src kinase, VAL201 aims to treat the cancer without causing the side effects. This is the direct consequence of VAL201 inhibiting only the protein-protein association of AR with Src kinase, without blocking formation of the AR–ER complex itself. The specificity of this action is expected to result in fewer side effects compared to those often seen with androgen deprivation therapy – loss of libido, erectile dysfunction, infertility, hot flushes, extreme tiredness, weight gain, strength and muscle loss, breast swelling, bone thinning, risk of heart disease, stroke and diabetes and mood swings.

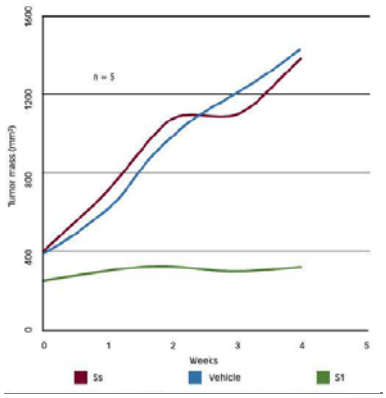
Furthermore, *in vitro* models have shown that VAL201 is effective in both hormone responsive and non-responsive prostate cancer, extending its therapeutic potential.

Pre-clinical studies

Cancer growth inhibition

In pre-clinical studies, VAL201 has been shown to produce a dose-dependent inhibition of tumour growth over a four week cycle of treatment, with a biological effect observed at 0.5mg/kg. Also, it was well tolerated up to 100mg/kg in several relevant species and no immunogenic effect was detected at the highest dose. These data also suggest that VAL201 would be a good candidate for use in combination with cytotoxic drugs.

VAL201 – xenograft study

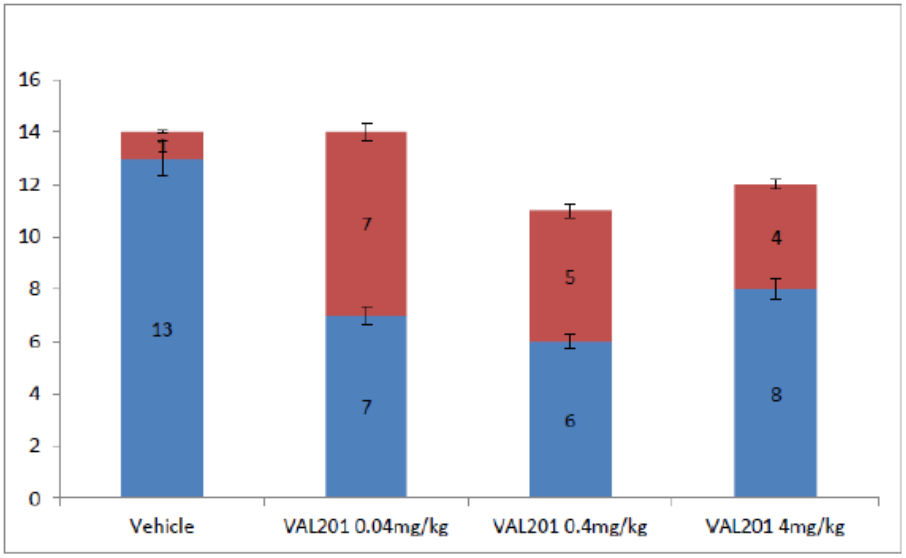


SS: Scramble sample, S1: VAL201
Source: European Oncology & Haematology

Anti-metastatic effect of VAL201

In addition to the anti-proliferative effect, in a subsequent xenograft study using PC3 prostate cancer cells, VAL201 may have an effect in reducing bone metastasis, a common feature in advanced prostate cancer patients. The following graph shows the number of metastases observed in prostate draining lymph nodes, demonstrating the efficacy of VAL201 in reducing the number of metastases compared to the vehicle.

VAL201 – Effect on lymph node metastasis



Bars indicate the number of lymph nodes with metastasis (blue) and without metastasis (red)
Source: ValiRx

Phase I/II clinical trial

Trial design

A Phase I/II clinical trial assesses the safety and tolerability of VAL201 in patients with advanced and metastatic prostate cancers

ValiRx is currently undertaking a Phase I/II open-label dose escalation study with VAL201, registered under the code name NCT02280317. The trial is assessing the safety and tolerability of VAL201 in up to 50 invited patients with advanced or metastatic prostate cancer. It is also targeting patients with advanced solid tumours for whom no effective standard therapy is available.

The study is divided into five cohorts, separated by dose, from 0.5mg/kg to 5mg/kg. VAL201 is being administered subcutaneously on days 1, 8 and 15 of a 21-day cycle, repeated up to six times for each patient.

- **Primary outcome:** Safety and tolerability of VAL201, and recording of any adverse events. Estimation of the maximum tolerated dose (MTD) and maximum administrated dose (MAD) within a timeframe of 18 weeks
- **Secondary outcome:** Evaluation of pharmacokinetic data and tumour activity following the RECIST (Response Evaluation Criteria in Solid Tumours) and/or PCWG2 (more specific to prostate cancer patients) criteria

Disclosed results

VAL201 has been proved to be safe and tolerated …

To date, no dose limiting toxicity has been observed and no serious adverse events related to VAL201 have been recorded in the 106 days median treatment duration. The main adverse effects observed have been a Grade 1 rash at the injection site, pain at the injection site and fatigue.

… with the final arm at higher dose currently recruiting

All patients in the first four cohorts have tolerated VAL201 very well and the fifth cohort (at 5mg/kg) has started recruiting recently.

- Preliminary data suggest that the study is meeting its primary outcomes of safety and tolerability criteria set for the trial for the first four cohorts
- Early results are really promising with seven patients who have completed the study showing no disease progression on CT imaging.
- Furthermore, 5/8 subjects have shown an improvement in prostate-specific antigen (PSA) doubling time (i.e. time taken for PSA level to double) following treatment with VAL201.

Analysis of samples is still ongoing, with still more subjects being followed.

Summary of results

Cohort	Dose (mg/kg)	Mean age	Mean days under dosing	Adverse events	Effect on PSA	Imaging response
1	0.5	71	191	G1 rash G1 fatigue	2.8x longer doubling time	SD/PD
2	1.0	63	126	G1 rash	Unchanged	SD
3	2.0	76	68	G1 rash G1 fatigue	Unchanged	SD, PD
4	4.0	70	88	G1 rash G1 fatigue	Reduction 0-40%, mean 25%	SD
5	5.0			To be recruited		

SD: stable disease, PD: progressive disease, G1: Grade 1
Source: ValiRx

The study is meeting its primary and secondary endpoint…

To date the study is meeting its primary and secondary endpoints, with good safety and tolerability at therapeutic levels of drug in advanced prostate cancer patients.

… with new centres added

ValiRx is accelerating recruitment by adding new study centres. This extension will have a wider scope for patient inclusion giving a stronger focus on the effects of VAL201 on advanced prostate cancer.

VAL401

- Lower development risk as product is a revised and improved formulation of a well-used currently marketed drug
- Phase II clinical trials in non-small cell lung cancer (NSCLC) in progress
- $300-400m per annum commercial opportunity based on a low pricing model

Description

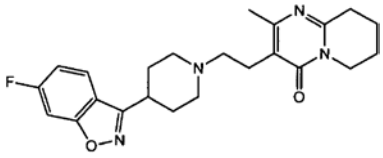
VAL401 is a new formulation of the known schizophrenic drug Risperdal, designed for cancer patients

ValiRx, together with its joint venture partner ValiSeek, is developing VAL401, which is a new formulation of risperidone (Risperdal, Johnson & Johnson), used for the treatment of schizophrenia. In contrast to the tablet formulation of Risperdal, VAL401 is a liquid lipid-filled capsule containing risperidone plus rumenic acid (a conjugated linoleic acid found in the fat of ruminants, in dairy products and some plant extracts). This formulation is patent protected and available in two doses – capsules containing 1mg and 5mg of risperidone.

Risperidone has already been used off-label in late-stage cancer patients, but hitherto for its psychotropic effect, in order to help patients to improve their quality of life, and to support them during chemotherapy. Therefore, with its advanced re-formulation, ValiRx has embarked upon a research programme with VAL401 in oncology to build on risperidone's palliative effects and prolong duration of life.

Risperidone

Structure of risperidone



Source: drug.com

Risperidone has been marketed for schizophrenia since 1992. A number of studies have shown that the molecule has an interaction with several receptors, including:

- **Dopamine:** D_2 and D_4 antagonist
- **Serotonin**: $5HT_{2a}$ and $5HT_{2c}$ antagonist
- **Histaminic**: H_1
- **Adrenergic:** $\alpha 1$ and $\alpha 2$ antagonist

Risperidone can also be used to treat patients with bipolar disorder as a monotherapy or a combination therapy with lithium or valproate. Although it is available generically, sales of the branded drug are still around $900m per annum.

Risperidone sales

Name	Company	Cumulative sales ($m)	Peak sales (2007) ($m)	2016 sales ($m)
Risperdal	Johnson & Johnson	44,045	4,548	893

Source: Company reports, Hardman & Co Life Sciences Research

The data published on risperidone enable ValiRx to accelerate the clinical research

During its commercial life, Risperdal has been associated with a number of common side effects, including sleepiness, increased weight, movement problems, and vision impairment, and some less common but more serious events including movement disorder, tardive dyskinesia and neuroleptic malignant syndrome. On the one hand, it is convenient to be using a core drug with a well-established pharmacokinetic and safety profile. On the other hand, ValiSeek is carrying out formal clinical trials in order to obtain an oncology label for VAL401, which will enable the wider anti-cancer and palliative effects of the risperidone containing formulation to be promoted in the clinic. The pharmacokinetic and side effect profile of VAL401 makes it very acceptable for use in cancer patients, with some of the common side effects such as weight gain and an increase in appetite even appreciated as positive effects in this patient population.

Mechanism of action

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

The anti-cancer activity of VAL401 was discovered at SEEK through the Magic Tag technology platform, which had previously been developed at the University of Warwick. Interestingly, it is considered that the anti-cancer activity is only present in the specific 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.

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

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.

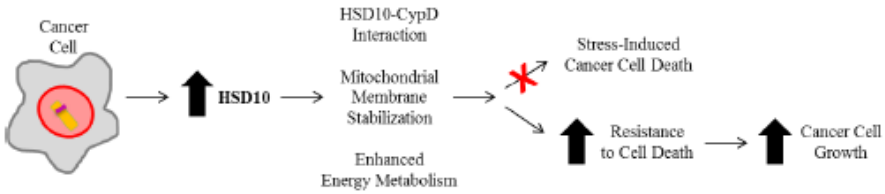
Importance of HSD10

HSD10 catalyses the reactions of a variety of substrates, such as β-hydroxybutyrate (BHB) and fatty acids, to propel mitochondrial respiration and increase ATP output. It has been shown to catalyse NADH-dependent redox reactions of many different substrates, including BHB, fatty acids, linear alcohols, branched short chain acyl-CoAs, amino acid catabolites, and steroids[1].

ValiRx is aiming at first in class with VAL401

While normally located in the mitochondria, HSD10 is overexpressed (approximately ten-fold) in cancer cells, where it is also accessible from the cytoplasm. Over-expression of HSD10 has been shown to provide a protective effect in cells undergoing nutritional stress[2]. Inhibition of HSD10 and its role in cancer seems to be a new area of exploration. A growing number of scientific publications have also demonstrated the over-expression of HSD10 and its survival effect in cancer cells.

Effect of HSD10 on cancer cell progression



Source: Emily Ann Carlson PhD thesis, 2016, University of Kansas

In cancer cells, increased HSD10 levels correlate with increased HSD10-CypD complex formation, enhanced mitochondrial membrane stabilisation, and enhanced energy production. This leads to cancer cell survival through higher cellular resistance to cell death, resulting in increased cancer cell growth.

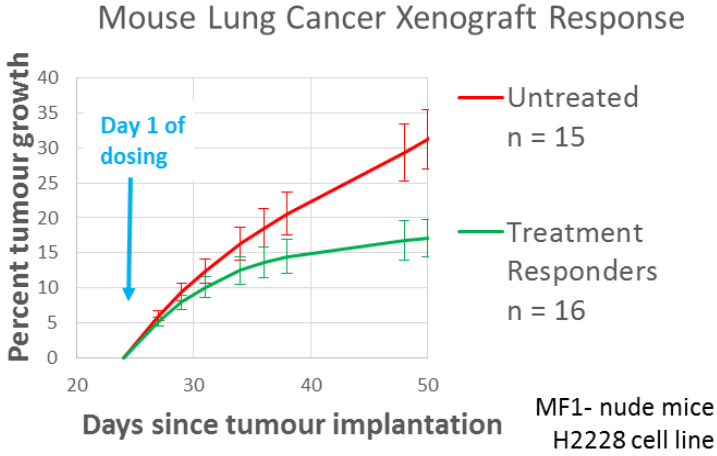
[1] Emily Ann Carlson, 2016
[2] Du Yan et al., 2000

Pre-clinical study

VAL401 shows in vitro and in vivo anti-cancer activities in NSCL, prostate and pancreatic cancers

Extensive existing data on risperidone is being referenced to progress VAL401 quickly. Pharmacokinetic analysis has shown that it has comparable properties to conventional risperidone. Pre-clinical studies with the new formulation have demonstrated efficacy in several *in vitro* and *in vivo* cancer models such as NSCLC, prostate cancer and pancreatic cancer, showing a reduced tumour growth rate and survival advantage. Initially, ValiRx will be targeting lung cancer with VAL401. Data from the mouse lung cancer model presented below shows a 50% inhibition of tumour growth in the H2228 cell line with 0.1 - 2 mg/kg.

VAL401 – Xenograft study



Source: ValiRx

High repeat dose toxicology studies in rats using 10mg/kg over 28 days showed no adverse events. These data, coupled to the historic data on risperidone, have enabled ValiRx to take VAL401 straight into Phase II clinical trials.

Phase II clinical trial

Historical data on Risperdal allow ValiRx to start a Phase II trial

In August 2016, ValiRx announced that its Phase II trial protocol had received acceptance by the regulatory authorities in Georgia, and the first non-small cell lung cancer patient was dosed orally with VAL401 in November 2016 at the Medulla Immunotherapy and Chemotherapy Clinic in Tbilisi. In order to accelerate the recruitment programme, two further sites in Georgia have been initiated with both JSC Neo Medi Clinic and the Research Institute of Clinical Medicine, recruiting patients.

Description

The trial, registered under the code name NCT02875340 (www.clinicaltrials.gove), is an open label study and will enrol a total of up to 20 patients with locally advanced or metastatic non-small cell lung cancer, after failure on at least one prior treatment.

- **Primary outcome:** Progression-free survival within a 6 month timeframe, assessed by RECIST criteria
- **Secondary outcome:** Patient quality of life, safety and tolerability, overall survival, adverse events, tumour response rate following RECIST criteria, and pharmacokinetic data will be assessed within a 6 month timeframe
- **Tertiary outcome:** Biomarker testing

Recruitment expected to complete in 2Q 2017 …

Recruitment is projected to be completed by end 2Q 2017, with a possible readout before end 2017. The target population for the study is lung cancer patients with 3-6 months life expectancy.

Patients are being recruited into a single cohort, which each receiving up to 10mg of VAL401 in a single dose per day. Each patient is acclimatised onto the drug regimen on an escalation starting at 2mg per day, and increasing at a rate of 2mg per day, until they reach either 10mg per day or their maximum tolerated dose if lower.

… with first data expected to be released in 3Q 2017

A recent amendment to the trial concerning a preliminary datalock will enable ValiRx to access data early from the trial and conduct mid-study analyses regarding safety, tolerability and pharmacokinetic data, with this data expected to be released in 3Q 2017.

Initial findings

First results coming from the clinic in Georgia are positive, with patients tolerating the treatment and pharmacokinetic data being continually accumulated.

Partnering

ValiSeek is currently looking for a licensing partner to help the passage of VAL401 beyond this Phase II study.

Pre-clinical pipeline

VAL301

- New formulation of VAL201 targeted at endometriosis
- Significant unmet medical need
- Plans to start Phase I clinical trial in 2018

Description

VAL301

VAL301 is a reformulated version of VAL201 targeting the gynaecologic condition endometriosis…

During pre-clinical work performed with VAL201, ValiRx identified a potential new indication for the compound, related to a gynaecological condition. VAL301 is a re-formulation of VAL201. Currently VAL301 is undergoing pre-clinical assessment for endometriosis, an indication for which, VAL301 is protected by a patent application. An increasing number of scientific publications have established a link between Src activation and endometriosis, which may lead to epithelial ovarian cancer[3].

Endometriosis

… affecting 6-10% of the female population…

Endometriosis is a benign gynaecological and oestrogen dependent condition characterised by the presence of endometrial-like tissue outside the uterus that results in debilitating pain, heavy or irregular periods, pain during or after sex, infertility, painful bowel movements, and fatigue. It is estimated to affect between 6-10% of pre-menopausal women[4], or about 5 million women in the US and 2 million in the UK. The economic burden of endometriosis for the UK alone is estimated at £8.2bn a year for treatment, loss of work and associated healthcare costs[5]. Despite the large number of sufferers, management of the condition is sub-optimal and includes:

- **Drugs:** most commonly pain killers and/or hormone treatments
- **Surgery:** excision or ablation of the endometrial lesion

… with poor disease management

The aim of most drug treatments is to reduce the pain with strong analgesics and/or suppress menstruation with hormone therapies. The aim of surgery is simply to ablate or remove the excess of endometrial tissue, however, problems can recur, especially if some endometrial tissue is left behind. Choice of treatment depends on the woman's priorities in terms of management of pain and/or fertility.

Pre-clinical data

Efficacy of VAL301 has been demonstrated in animal study and exhibited less side effect compare standard of care

VAL301 has been shown to reduce abnormal endometrial growth, whilst leaving other hormone-induced activities working normally. *In vitro* experiments initiated by ValiRx show a reduction of 50% in endometrial lesion size directly related to dose and five generations of offspring have been produced with treated animals. This suggests that VAL301 does not affect fertility the same way existing treatments do. Also, a pre-clinical study in an animal model indicates that VAL301 should not affect bone density, an effect often reported with hormone therapies.

Comforted by these results, ValiRx is currently completing further pre-clinical work and preparing protocols and submission paperwork for clinical trials in endometriosis. Our intention is to report on this opportunity closer to the initiation in 2018.

[3] Manek et al., 2016
[4] National Institute of Health
[5] www.endometriosis-uk.org

VAL101

- VAL101 is a proprietary Bcl-2 gene silencing platform
- Potential to target several indications in oncological and neurological fields

VAL101

VAL101 is a gene silencing therapeutic in pre-clinical evaluation in cancer

One of the main characteristics of cancer cells is the over-expression and/or the aberrant expression of certain genes that promote cell growth. VAL101 targets and silences the gene that expresses Bcl-2, an oncogenic protein that plays a crucial role in cell death regulation. When Bcl-2 is over-expressed, it may inhibit pro-apoptotic signals, allowing the cancer cell to survive under stressful conditions.

GeneICE utilises a natural gene regulation process that cells use to express or halt the expression of a gene. Unlike the traditional lengthy and costly drug discovery approach in finding a protein inhibitor, GeneICE would directly silence the selected gene. Presently, VAL101 is in pre-clinical evaluation.

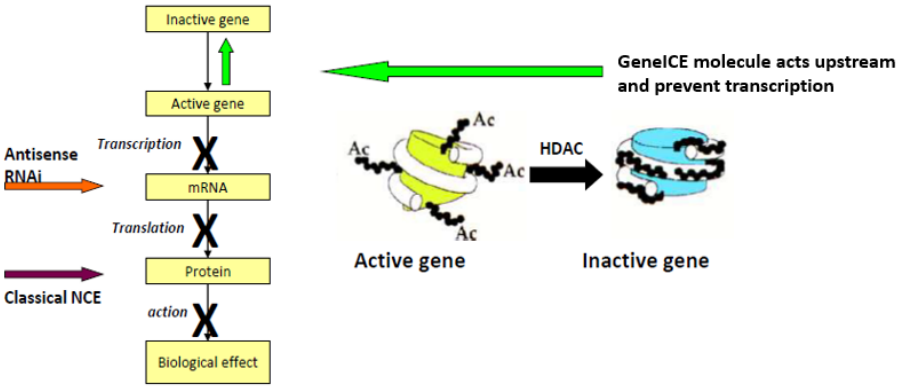
GeneICE Platform

GeneICE is ValiRx proprietary gene silencing platform that mimic the natural process of inhibiting gene

GeneICE (Gene Inactivation by Chromatin Engineering) is a novel proprietary gene silencing platform for the efficient silencing of targeted genes. This technology is based on natural mechanisms and has the potential to halt and reverse tumour growth. ValiRx has attracted two Eurostars grants, a European grant scheme of EUR1.6m each, for further development of its GeneICE technology platform.

As depicted in the following scheme, GeneICE is mimicking a natural process in cells to silence genes. The technology acts upstream of the gene expression, potentially enabling a better inhibition compared to existing therapeutics acting at the protein or post-transcriptional levels.

GeneICE mechanism



NCE: New Chemical Entity
Source: ValiRx

GeneICE construct is an epigenetic alternative to antisense and RNAi technologies. It consists of two molecule constructs with two distinct functions:

- An oligonucleotide component that targets directly the gene of choice by binding to it by complementarity
- A peptide component that binds HDAC proteins. By doing so, the de-acetylation process stops the gene being expressed by preventing the transcription

Commercial opportunity

Prostate cancer – VAL201

Aetiology and prevalence

Prostate cancer is the third most common type of cancer…

Androgens (mainly testosterone and dihydrotestosterone) are required for normal growth and function of the prostate. They are also necessary for prostate cancers to grow. Androgens promote growth of both normal and cancerous prostate cells by binding to and activating the androgen receptor, thereby stimulating the expression of specific genes that cause prostate cells to grow.

… with 40,000 new cases diagnosed every year

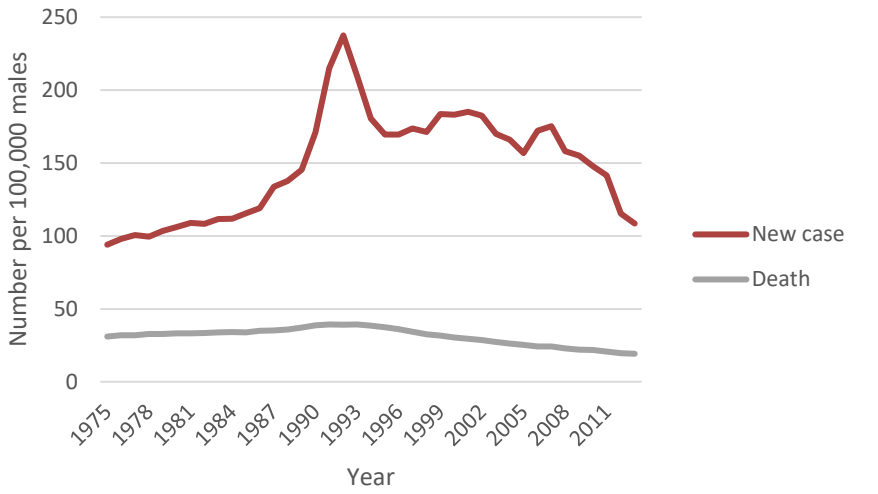
Early in their development, prostate cancers need relatively high levels of androgens to grow. Such tumours are referred to as androgen dependent (or androgen sensitive) because treatments that decrease androgen levels or block androgen activity can inhibit their growth.

VAL201 targets patients affected by advanced and metastatic prostate cancers where there is a high unmet medical need

Prostate cancer is the third most common type of cancer after breast and lung and represents 9.6% of all new cancer diagnoses in the US[6], and in the UK 40,000 new cases are diagnosed every year[7]. It is characterised by very slow growth and is usually diagnosed late in men, with a median age at diagnosis of 66 years and at death of 80 years. In 79.2% of diagnoses, the cancer remains localised, which generates good outcomes initially with 5 year survival rates of 98.9%[6]. However, it is when the cancer becomes advanced and metastasises that the statistics deteriorate, with the five-year survival rate falling 29.8%[6].

Initially, it is expected that VAL201 would be targeted at patients with advanced prostate cancer, but longer-term its mechanism of action suggests that it could be used much earlier than current therapies and potentially for preventive reasons.

Prostate cancer in the US



Source: National Institute of Health: National Cancer Institute

[6] NCI-NIH
[7] NHS

Current treatment paradigm

Treatment choice in prostate cancer is dependent on the progression stage

Choice of treatment, if any, is dependent on the stage of the cancer.

Watchful waiting: Physicians and patients decide to delay palliative treatment and, instead, monitor the tumour's development, only initiating treatment when it is judged to be of likely benefit. This is usual for patients with localised disease.

Active surveillance: Active surveillance is where no treatment is needed but the tumour is monitored through biopsy, prostate-specific antigen (PSA) tests and/or scans. Because prostate cancer is slow growing and consequently appears 'benign', only about one-third of patients receive treatment due to progression[8], thereby delaying any treatment related side effects.

PSA test

PSA tests are run routinely and level are not entirely specific to prostate cancer. PSA levels are raised by multiple factors such as non-cancerous growth of the prostate known as benign prostatic hyperplasia (BPH), an infection of the urinary tract, or due to inflammation of the prostate, as well as other natural or non-natural causes. Additionally, it can fluctuate from month to month.

Clinical landscape

The global prostate cancer therapeutics market is segmented into hormone therapy, chemotherapy, biologic therapy, and targeted therapy. Of these, the hormone therapy segment has dominated the global prostate cancer therapeutics market and is forecast to remain unaffected. Recently launched and high-priced targeted therapies (biotherapeutics like Sipuleucel-T) have significantly increased both the size of the market and hence the market share.

Hormone therapy

Hormone therapy dominates the prostate cancer therapeutic market, with many options acting at the androgen level

Traditional hormone therapy (also called androgen deprivation therapy) is often very effective at shrinking or slowing the growth of prostate cancer that has spread. The aim is to reduce (or eliminate) levels of male hormones from affecting prostate cancer cells. Most patients respond well initially, but become resistant to these drugs over a period of months or years. When prostate cancer becomes hormone resistant, the prognosis is poor with nearly 90% of patients suffering disease recurrence with bone metastases, reducing survival dramatically[9].

Treatments to lower androgen levels: Luteinizing hormone-releasing hormone (LHRH) agonists reduce the production of testosterone and are used in advanced prostate cancer, together with radiotherapy and surgery, for patients with localised disease who have poor prognosis.

Treatments to lower androgen levels

Generic	Brand	Marketer	2016 sales ($m)	Cumulative ($m)
LHRH agonists				
Leuprolide	Lupron	Takeda	*1,028	*24,269
Goserelin	Zoladex	AstraZeneca	816	20,118
GnRH antagonist				
Degarelix	Firmagon	Ferring		

**2015 sales data*
Source: Hardman & Co Life Sciences Research

[8] American Cancer Society
[9] S.J. Hotte, F. Saad, Current management of castrate-resistant prostate cancer Curr Oncol. 2010 Sep; 17(Suppl 2): S72–S79.

Treatments to stop androgen secretion: Steroidal or non-steroidal anti-androgens block androgen receptors. They act in different ways: the non-steroidal compete with androgens at the receptor level, while steroidal anti-androgens also have central inhibition of the pituitary gland, inhibiting the production of gonadotrophins.

Anti-androgens

Generic	Brand	Marketer	2016 sales ($m)	Cumulative ($m)
Flutamide	Eulexin	Merck	generic	2,352
Bicalutamide	Casodex	AstraZeneca	247	12,970
Enzalutamide	Xtandi	Astellas	*2,083	6,188
CYP17 inhibitor				
Abiraterone	Zytiga	J&J	2,260	9,688

**2015 sales data*

Source: Hardman & Co Life Sciences Research

Positioning VAL201

Due to its mechanism of action, VAL201 may be used across the whole spectrum of prostate cancer…

The mode of action of VAL201 opens up the possibility of the drug being used across the whole spectrum of prostate cancer, even during the 'watchful waiting' and 'active surveillance' periods. This opens the product up to a much larger potential market. If ValiRx confirms the efficacy of VAL201 in both hormone-sensitive and hormone-resistant prostate cancer, coupled with its very low side effect profile seen to date, it would suggests that the drug is sufficiently versatile to be used earlier than current therapies in an attempt to prolong the watchful waiting/active surveillance period.

Addressable market

…addressing a market worth above $2bn

Our assumptions are based on the number of prostate cancer patients published by the National Cancer Institute (US) and Eurostat (EU). Based on current schedules, VAL201 could be on the market around 2023. Our model assumes that it would be competitively priced, but also affordable to allow its earlier use, which would equate to about $4,000 per annum per patient. Ultimately, the decision of price will be made by ValiRx's eventual commercial partner, with the backing of good clinical data. On the basis that VAL201 will be used at all stages of the disease, the addressable market is very large and suggests that the drug would generate annual sales comfortably above $2bn.

VAL201 sales model

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7	Year 8	Year 9	Year 10	Year 11	Year 12
Europe												
Addressable market ($m)	26,400	26,664	26,931	27,200	27,472	27,747	28,024	28,304	28,587	28,873	29,162	29,454
Market share (%)	1%	2%	3%	4%	5%	6%	7%	8%	9%	10%	10%	10%
Sales ($m)	**264**	**533**	**808**	**1,088**	**1,374**	**1,665**	**1,962**	**2,264**	**2,573**	**2,887**	**2,916**	**2,945**
United States												
Addressable market ($m)	11,600	11,716	11,833	11,951	12,071	12,192	12,314	12,437	12,561	12,687	12,814	12,942
Market share (%)	1%	2%	3%	4%	5%	6%	7%	8%	9%	10%	10%	10%
Sales ($m)	**116**	**234**	**355**	**478**	**604**	**732**	**862**	**995**	**1,131**	**1,269**	**1,281**	**1,294**
Global												
Total in-market sales ($m)	380	768	1,163	1,566	1,977	2,396	2,824	3,259	3,703	4,156	4,198	4,240
Net sales* ($m)	296	599	907	1,221	1,542	1,869	2,202	2,542	2,888	3,241	3,274	3,306
Net sales (£m)	**228**	**460**	**698**	**940**	**1,186**	**1,438**	**1,694**	**1,955**	**2,222**	**2,493**	**2,518**	**2,543**

**After average wholesaler discounts*

GBP/US$: 1.300

Source: Hardman & Co Life Sciences Research

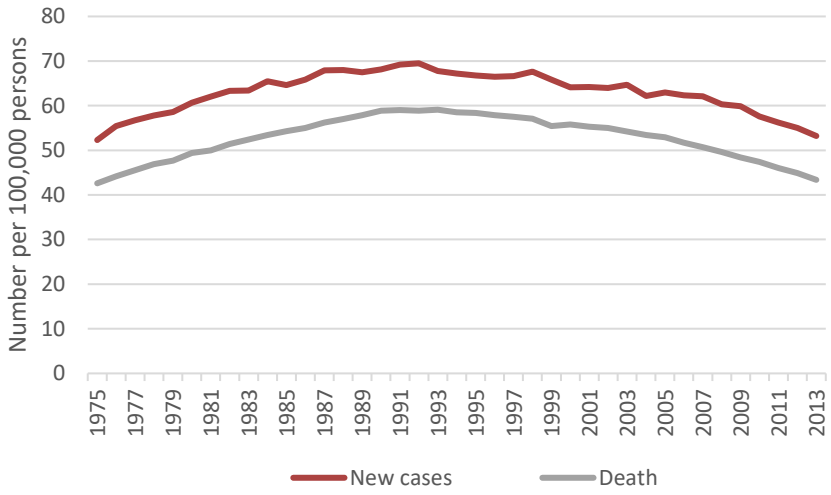
NSCLC – VAL401

Lung cancer is the leading type of cancer…

NSCLC accounts for over 85% of all lung cancers and is a leading cause of death. There are more than 220,000 new cases in the US annually and 150,000 deaths. This type of lung cancer occurs mainly in current, former or passive smokers. The graph below shows the number of new NSCLC cases per 100,000 of population. It demonstrates clearly the very poor prognosis of people with this condition with a five year survival rate of only 17.7%.

… with a very poor prognosis due to late diagnosis

Number of NSCL cancer per 100,000 persons in the US



Source: www.cancer.gov

Despite better understanding of lung cancer and the increased number of available drugs, the graph indicates that there has been little improvement in the survival rate from this type of cancer, with surgery remaining the only treatment option. The poor prognosis with NSCLC is often attributed to the fact that diagnosis is made only when the disease is well advanced and established.

Non-small cell lung cancer can be subdivided in 3 different types:

- **Adenocarcinoma** – Accounting for 40% of the lung cancer, adenocarcinoma has the characteristic to grow slower than other type of lung cancer and, as such, tends to have a better prognosis. They are usually found in the outer part of the lung
- **Squamous cell carcinoma** – They are located inside the airways of the lung
- **Large cell carcinoma** – It can appear in any part of the lung and tends to grow and spread quickly

Depending on the stage of the cancer, five treatment options exist for people with NSCLC:

- Surgery, with the ablation of cancerous tissues.
- Radiation therapy
- Chemotherapy
- Immunotherapy
- Radiofrequency therapy

NSCLC market

Hardman & Co estimates that the global market for drugs to treat lung cancer was ca.$7.0bn in 2015, and the market looks set to grow 8-13% over the next five years to $11-12bn. The current standard of care is Avastin (used also in other conditions; Roche), which dominates the market with sales of ca.$7bn in 2015 and cumulative sales of $57.2bn since launch, together with an old drug, Taxotere (BMS). The advanced NSCLC market is thought to account for 80% of all lung cancer cases.

The setback seen by BMS highlights the need for more efficacious therapies

The market for NSCLC drugs had been expected to grow substantially over the next five years following the launch of PD-L1 inhibitors. However, they received a significant setback recently, when Opdivo (BMS) was found to be no better that chemotherapy in a study of 541 treatment naïve patients newly diagnosed with advanced lung cancer (CheckMate-026; BMS website 5th August 2016). The study end-point was a delay in disease progression or death compared to chemotherapy; however, this goal was missed. The results were a surprise to the market because in a similarly designed study, Keytruda (pembrolizumab, PD-1 inhibitor, Merck & Co) had previously been shown to delay disease progression in newly diagnosed drug naïve NSCLC patients.

The NSCLC is a high unmet medical need and further therapeutic options needed

These results, together with the high incidence and poor prognosis for NSCLC, demonstrate that it is a market of unmet need and with the very high death incidence. The NSCL cancer market is desperately in need of a new and effective drug. In 2013, there were an estimated 416,000 people living with lung and bronchus cancer in the United States.

With 20 approved and well established drugs used currently in NSCLC and with more than 354 open studies registered[10], VAL401 would be entering an even more crowded market. Again, we are of the opinion that ValiRx will likely out-license this asset for late-stage clinical trials and commercialisation.

Ranking of NSCL cancer approved drugs

Rank	Name	Drug	Company	MoA	2016 sales	Cumulative
1	Avastin	Bevacizumab	Roche	VEGF Recombinant human mAb	$6,886m	$64,091m
2	Alimta	Pemetrexed	Eli Lilly	Folate antimetabolite	$2,283m	$22,468m
3	Afinitor	Everolimus	Novartis	mTOR inhibitor	$1,516m	$7,561m
4	Tarceva	Erlotinib	Roche	EGFR kinase inhibitor	$1,040m	$13,382m
5	Abraxane	Paclitaxel	Abraxis/Celgene	Anti-mitotic	$973m	$4,322m
6	Iressa	Gefitinib	AstraZeneca	EGFR kinase inhibitor	$513m	$5,878m
7	Opdivo	Nivolumab	BMS	PD-1 humanised mAb	$3,774m	$4,722m
8	Xalkori	Crizotinib	Pfizer	ALK kinase inhibitor	$561m	$1,893m
9	Cyramza	Ramucirumab	Eli Lilly	VEGFR fully humanised mAb	$614m	$1,097m
10	Taxotere	Docetaxel	Sanofi	Anti-mitotic	$198m	$26,109m
11	Gemzar	Gemcitabine	Eli Lilly	Nucleoside analogue	$111m	$15,274m
12	Zykadia	Ceritinib	Novartis	ALK kinase inhibitor	$91m	$201m
	Tagrisso	Osimertinib	AstraZeneca	EGFR kinase inhibitor	$423m	$442m
	Portrazza	Nicitumumab	Lilly	EGFR Recombinant human mAb	$15m	$15m
	-	Methotrexate	Generic	Folate antimetabolite	Used since 1950	
	Alecensa	Alectinib	Roche	ALK kinase inhibitor	$185m	$252m
	Gilotrif	Afatinib	B. Ingelheim	EGFR and HER2 kinase inhibitor	N/A	
	Paclitaxel	Taxol	Generic	Anti-mitotic	N/A	
	Paraplatin	Carboplatin	Generic	DNA-Alkylating agent	N/A	

Source: Hardman & Co Life Sciences Research

[10] www.cancer.gov

Addressable market

VAL401 will target the 2nd line therapeutic segment…

There will clearly have to be a decision to be made at an appropriate time, based on balancing an attractive price that gains high market share against an aggressive price that may limit market share. The key, therefore, will be the efficacy and survival data. For the purposes of modelling we have assumed an annual price of $25k per patient for VAL401.

…with a price tag evaluated at $25,000…

With VAL401, ValiRx and its partner ValiSeek will first target the second line therapeutic segment in NSCLC, probably in combination with a folate anti-metabolite such as pemetrexed (Alimta, Lilly). Given that VAL401 is 'simply' a new complex formulation of an existing drug for a new indication, the issue for the commercial partner will be that of price, with the price for traditional risperidone having set a benchmark. However, proven efficacy for VAL401 would allow it to be priced competitively against existing second line therapies for NSCLC, which currently stand in the range $30,000-50,000 p.a.

… expected to reach market around 2022

Our assumptions are based on the number of lung cancer patients published by the National Cancer Institute (US) and Eurostat (EU). On current schedules, VAL401 could be on the market around 2022. Our pricing assumption is for an attractive price at the bottom-end of the range for current second-line therapies in order to achieve good market penetration, which will be helped by the extensive safety data already available for the marketed product. On this basis, VAL401 should comfortably achieve annual net sales in excess of $1.0bn.

VAL401 sales model

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7	Year8	Year9	Year 10	Year 11	Year 12
Europe												
Addressable market ($m)	11,720	11,837	11,956	12,075	12,196	12,318	12,441	12,565	12,691	12,818	12,946	13,076
Market share	1%	2%	3%	4%	5%	6%	7%	8%	9%	10%	10%	10%
Sales ($m)	**59**	**237**	**359**	**483**	**610**	**739**	**871**	**1,005**	**1,142**	**1,282**	**1,295**	**1,308**
United States												
Addressable market ($m)	8,300	8,383	8,467	8,551	8,637	8,723	8,811	8,899	8,988	9,078	9,168	9,260
Market share	1%	2%	3%	4%	5%	6%	7%	8%	9%	10%	10%	10%
Sales ($m)	**83**	**168**	**254**	**342**	**432**	**523**	**617**	**712**	**809**	**908**	**917**	**926**
Global												
Total in-market sales ($m)	142	404	613	825	1,042	1,262	1,488	1,717	1,951	2,190	2,211	2,234
Net sales* ($m)	106	310	470	633	799	969	1,141	1,318	1,497	1,680	1,697	1,714
Net sales (£m)	**81**	**239**	**362**	**487**	**615**	**745**	**878**	**1,014**	**1,152**	**1,292**	**1,305**	**1,318**

**After average wholesaler discounts*
GBP/US$: 1.300
Source: Hardman & Co Life Sciences Research

Financials & Investment case

ValiRx is a virtual company with most of its activity being outsourced.

Profit & Loss

In the medium term, the P&L account is driven by two numbers, the corporate overhead/administration costs and the investment in R&D/clinical trials.

- **Sales** – The company is currently not revenue generating. ValiRx sold its subsidiary ValiFinn for €800,000 (£714,286) on 31st October 2016. ValiRx still retains a licence to use the TRAC technology in its therapeutic developments
- **SG&A** – The underlying corporate overhead have not changed materially since 2013. They are expected to rise in-line with inflation
- **R&D** – Investment is rising as a consequence of the two clinical trials currently running and the extension to other trial sites. Trial costs have been allocated evenly across the anticipated trial timelines
- **Tax credit** – ValiRx is accruing and receiving tax credits from the UK government in relation to its R&D spend

Profit & Loss account

Year end Dec (£000)	2014	2015	2016	2017E	2018E	2019E
Sales	88	83	0	0	0	0
COGS	-61	-78	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
Depreciation	-1	-11	-11	-5	-11	-5
Other income	211	203	0	0	0	0
Underlying EBIT	**-2,958**	**-2,888**	**-3,949**	**-4,508**	**-5,165**	**-5,941**
Amortisation	-91	-92	-92	-92	-92	-92
Share based costs	-89	-49	-128	-134	-141	-148
Exceptional items	0	0	183	183	0	0
Statutory EBIT	-3,138	-3,029	-3,987	-4,734	-5,399	-6,182
Net financials	-503	462	-1,582	-114	-126	-150
U/L pre-tax profit	**-2,952**	**-2,889**	**-5,531**	**-4,622**	**-5,292**	**-6,092**
Reported pre-tax	-3,641	-2,567	-5,569	-4,848	-5,525	-6,332
Tax liability/credit	397	391	620	744	893	1,072
Tax rate	-11%	-15%	-11%	-15%	-16%	-17%
Underlying net income	**-2,470**	**-2,440**	**-4,711**	**-3,877**	**-4,399**	**-5,020**
Statutory net income	-3,160	-2,118	-4,748	-4,104	-4,632	-5,261
Ordinary shares (m):						
Period-end	23.32	38.34	133.36	132.16	132.16	132.16
Weighted average	23.43	31.79	57.74	113.55	132.16	132.16
Fully diluted	26.01	35.53	61.48	117.29	135.90	135.90
Underlying basic EPS (p)	**-10.5**	**-7.7**	**-8.2**	**-3.4**	**-3.3**	**-3.8**
Statutory Basic EPS (p)	-13.5	-6.7	-8.2	-3.6	-3.5	-4.0
U/l Fully-diluted EPS (p)	**-9.5**	**-6.9**	**-7.7**	**-3.3**	**-3.2**	**-3.7**
Stat. Fully-diluted EPS (p)	-12.2	-6.0	-7.7	-3.5	-3.4	-3.9
DPS (p)	0.0	0.0	0.0	0.0	0.0	0.0

Source: Hardman & Co Life Sciences Research

Balance sheet

- **Net cash/(debt)** – at 31st December 2016, ValiRx had net debt of £732k on its balance sheet, comprising cash of £561k and outstanding convertible loan notes of £1,294k/$1,592k, which are treated as debt, although in all likelihood these will be converted into shares
- **Current cash** – Following the capital raise in March, less the monthly cashburn, the current cash position is forecast to be about £0.5m
- To continue funding R&D investment at current levels, further capital will be required during 2017. This could come either from licensing agreements, collaborative deals with equity components and/or an equity placing by the company

Balance sheet

at 31st Dec (£000)	2014	2015	2016	2017E	2018E	2019E
Shareholders' funds	2,762	4,533	2,369	-1,735	-6,366	-11,627
Cumulated goodwill	0	0	0	0	0	0
Total equity	2,762	4,533	2,369	-1,735	-6,366	-11,627
Share capital	7,282	8,121	8,166	8,166	8,166	8,166
Reserves	-4,520	-3,667	-5,816	-9,920	-14,552	-19,812
Minorities	26	79	20	20	20	20
Provisions/liabilities	0	0	0	0	0	0
Deferred tax	0	0	0	0	0	0
Long-term debt	0	0	0	0	0	0
Short-term loans	0	0	1,294	1,294	1,294	1,294
less: Cash	453	232	561	-1,930	-6,779	-12,270
less: Deposits	0	0	0	0	0	0
less: Non-core invests.	0	1,463	97	0	0	0
Invested capital	**2,335**	**2,837**	**3,006**	**1,490**	**1,707**	**1,937**
Fixed assets	2	22	11	5	-5	-11
Intangible assets	2,380	2,673	2,825	2,895	2,968	0
Inventories	11	44	0	0	0	0
Trade debtors	*18*	*33*	*0*	*0*	*0*	*0*
Other debtors	*363*	*253*	*781*	*731*	*731*	*731*
Tax credit/liability	*397*	*400*	*644*	*682*	*819*	*982*
Trade creditors	*-514*	*-448*	*-1,127*	*-563*	*-563*	*-563*
Other creditors	*-321*	*-141*	*-127*	*-691*	*-691*	*-691*
Debtors less creditors	-57	98	171	159	295	459
Invested capital	**2,335**	**2,837**	**3,006**	**1,490**	**1,707**	**1,937**
Net cash/(debt)	**453**	**232**	**-734**	**-3,224**	**-8,073**	**-13,564**

Source: Hardman & Co Life Sciences Research

Cashflow

- **Convertible Loan Notes** – During 2016, ValiRx issued £3.0m (gross) CLNs to Yorkville and Bracknor, of which £1.7m had been converted into Ordinary shares by the year end
- **Capital increase** – ValiRx raised £1,200k gross (£1,090 net) by the way of a Placing in March 2017
- To fund the business over the next two years, we forecast a minimum cash requirement of c.£6.7m which could come from licensing up-front payments, equity participation in a collaborative deal, an equity fund raise or a combination thereof

Cashflow

Year end Dec (£000)	2014	2015	2016	2017E	2018E	2019E
Trading profit	-2,958	-2,888	-3,949	-4,508	-5,165	-5,941
Depreciation	1	11	11	5	11	5
Inventories	*-7*	*-33*	*12*	*0*	*0*	*0*
Receivables	*-200*	*95*	*-1,072*	*0*	*0*	*0*
Payables	*-159*	*-167*	*788*	*563*	*0*	*0*
Change in working capital	-366	-105	-272	563	0	0
Exceptionals/provisions	7	5	-22	0	0	0
Other	0	0	0	0	0	0
Company op cashflow	**-3,317**	**-2,977**	**-4,233**	**-3,939**	**-5,155**	**-5,936**
Net interest	6	-1	-338	3	-10	-33
Tax paid/received	310	388	376	682	819	982
Operational cashflow	**-3,001**	**-2,590**	**-4,196**	**-3,254**	**-4,346**	**-4,987**
Capital expenditure	-1	-32	0	0	0	0
Sale of fixed assets	0	0	0	0	0	0
Free cashflow	**-3,002**	**-2,622**	**-4,196**	**-4,196**	**-4,346**	**-4,987**
Dividends	0	0	0	0	0	0
Acquisitions	-274	-390	-387	-387	-387	-387
Disposals	331	0	3	0	0	0
Other investments	-72	110	998	998	0	0
Cashflow after invests.	**-3,017**	**-2,901**	**-3,581**	**-3,581**	**-4,733**	**-5,374**
Share repurchases	0	0	0	0	0	0
Capital increases	2,510	2,681	3,909	1,090	0	0
Currency effect	0	0	0	0	0	0
Cash/(debt) acquires	0	0	0	0	0	0
Change in net debt	**-507**	**-220**	**328**	**-2,491**	**-4,733**	**-5,374**
Hardman FCF/share (p)	-12.8	-8.1	-7.3	-2.8	-3.3	-3.7
Opening net cash	960	453	232	561	-1,930	-6,662
Closing net cash	**453**	**232**	**561**	**-1,930**	**-6,662**	**-12,036**

Source: Hardman & Co Life Sciences Research

Valuation

Discounted cashflow

The best approach to valuing biopharmaceutical companies is to prepare detailed discounted cashflow analyses of key products through to patent expiry, and then to risk-adjust the NPV based upon industry standards for the probability of the product reaching the market. Whilst this is possible for ValiRx, its assets are at a relatively early stage and late-stage development work and commercialisation is dependent on the signing of a licensing deal with a big partner, who will ultimately determine the pricing of the products, which, in turn, will determine the likely market penetration. Therefore, there are big question marks over the reliability of such a DCF valuation.

A DCF valuation has been applied for VAL201 and VAL401…

Having said that, in order to give readers an idea of valuation generated by DCF, the DCF model has been applied to ValiRx's two clinical candidates, VAL201 and VAL401, based on the commercial opportunity numbers provided in the tables on pages 20 and 22, respectively, and the following assumptions:

DCF assumptions

	VAL201	VAL401
Time to launch	6 years	5 years
Price of drug per annum (est)	$4,000	$25,000
Market penetration	Low	Low
Royalty rate	10%	10%
WACC	10%	10%
Costs offset by up-front receipts	✓	✓
Risk adjustment	5%	10%
NPV of royalty stream (£m)	**24.5**	**18.3***
R&D spend to licensing deal (£m)	-6.0	-5.0
Risk-adjusted NPV (£m)	**18.5**	**13.3**

**After allowing for 40% to ValiSeek*
Source: Hardman & Co Life Sciences Research

… providing a combined risk-adjusted NPV of £31.8m

Based on these simple assumptions, the NPV of the royalty streams for ValiRx's share of VAL201 and VAL401 through to patent expiry are £18.5m and £13.3m respectively. Combining them gives a risk-adjusted NPV of £31.8m, which is 10.4x the current market capitalisation, or 8.4x the current EV. This figure is for these two drug candidates alone and any other products in the ValiRx pipeline would be additional to this valuation.

An important consideration discussed earlier is the price that is likely to be charged per patient per annum for VAL401. Our forecasts have assumed an annual price of $25k. For every $5k difference in this price, the valuation alters by ±£3.6m.

Comparative valuation

Given the attention being paid to oncology R&D, there is no shortage of small cap pharmaceutical companies, both in the UK and on a global basis, that are working on the early stage of clinical development, against which ValiRx can be compared.

UK peer comparisons

The table below shows a number of AIM listed development companies. Most are operating in the field of oncology, plus Diurnal (speciality pharma with a regulatory submission) and Evgen (similar risk product at similar stage of development). Enterprise values are in the range 1.8x to 52.9x that of ValiRx suggesting the market is undervaluing the group.

UK peer group valuations							
Company	**Diurnal**	**Evgen**	**Sareum**	**Silence Ther.**	**Scancell**	**Tiziana**	**ValiRx**
Ticker	**DNL**	**EVG**	**SAR**	**SLN**	**SCLP**	**TILS**	**VAL**
Share price	128.5	19.3	0.9	96.0	10.9	203.9	2.30
Shares in issue (m)	52.2	73.3	2,645.2	70.0	261.6	96.2	133.4
Mkt cap (£m)	**67.1**	**14.1**	**23.3**	**67.2**	**28.5**	**196.1**	**3.07**
Cash	30.1	7.1	2.3	39.0	6.5	8.3	0.56
Debt	-3.2	0.0	0.0	0.0	0.0	-13.1	-1.29
EV (£m)	**40.2**	**7.0**	**21.0**	**28.2**	**22.0**	**200.9**	**3.80**
Relative EV	10.6x	1.8x	5.5x	7.4x	5.8x	52.9x	-
Stage of development	Regulatory	Phase II	Phase I/II	Phase II	Phase I/II	Phase I/II	Phase I/II

Prices taken at close of business on 26th May 2017
Source: Hardman & Co Life Sciences Research

Global peer comparisons

The difference in valuation ascribed by markets is even wider when comparing ValiRx with a number of global development companies in the field of oncology, where the relative enterprise value range is 0.2x to 276.5x that of ValiRx.

Global peer group valuations								
Company	**Advaxis**	**Bavarian Nordic**	**Galena Biopharma**	**Inovio**	**OncoSec Med**	**OSE Immuno**	**Scancell**	**ValiRx**
Ticker	**ADXS**	BAVA	**GALE**	**INO**	**ONCS**	**OSE**	**SCLP**	**VAL**
Local currency (lc)	$	NKR	$	$	$	€	£	£
Share price	8.4	350.5	0.56	7.9	1.05	6.9	10.9	2.30
Shares in issue (m)	40.3	30.9	53.0	74.3	20.9	14.3	261.6	133.4
Market cap (lc)	339.7	10,842.4	29.7	585.6	21.9	98.0	28.5	3.07
Mkt cap (£m)	**271.1**	**1,264.1**	**23.7**	**467.4**	**17.5**	**92.3**	**28.5**	**3.07**
Cash	78.7	1,502.0	29.1	134.6	24.1	25.3	6.5	0.56
Debt	-0.4	0.0	-13.6	0.0	-3.2	0.0	0.0	-1.29
EV (lc)	261.4	9,340.4	14.2	451.1	1.0	72.7	22.0	3.80
EV (£m)	**208.6**	**1,089.0**	**11.3**	**360.0**	**0.8**	**68.5**	**22.0**	**3.80**
Relative EV	53.0x	276.5x	2.9x	91.4x	0.2x	17.4x	5.6x	-

lc = local currency
Prices taken at close of business on 26th May 2017
Source: Hardman & Co Life Sciences Research

Taken together, both methods of valuation – DCF and peer comparison – indicate that ValiRx is being undervalued by the market. It's current market capitalisation is about one-eighth of the ca.£23m that has been invested in the company to date. The question, therefore, is why?

In our opinion, there are two reasons for this. First, ValiRx will need more capital to move its pipeline forward and the market is well aware of this, but this situation is also true for most of its peers. Secondly, the shareholder base of ValiRx is mostly high net worth individuals, with the only institutional-type recent shareholders being Yorkville and Bracknor, which were both there through convertible loan note conversions for the very reason that Valirx's valuation represents a significant opportunity. In order for ValiRx to move forward, it must attract an increased number of well-recognised deep-pocketed institutional shareholders.

Company matters

Registration

Incorporated in the UK with company registration number: 3916791

3rd Floor
16 Upper Woburn Place
London, WC1H 0BS
UK

Tel: +44 (0)20 3008 4416
Fax: +44 (0)20 3008 4415

Email: info@ValiRx.com

Board of Directors

Board of Directors			
Position	**Name**	**Remuneration**	**Audit**
Chairman	Oliver de Giorgio-Miller	M	
Chief Executive Officer	Dr Satu Vainikka		
Chief Financial Officer	Gerry Desler		M
Chief Operations Officer	Dr George Morris		M
Non-executive director	Kevin Alexander	M	
Non-executive director	Seppo Mäkinen		

M = member; C = chair
Source: Company reports

Oliver de Giorgio-Miller – Non-executive Chairman

Oliver has experience in the management and commercial advancement of life science companies, having worked for over 30 years with several global pharmaceutical and medical device companies including Schering AG, Roche, Intavent-Orthofix and Photo Therapeutics, a Cancer Research UK company. Formerly a city analyst covering early stage biopharmaceutical and medical device companies.

Dr Satu Vainikka – Chief Executive Officer

Satu has many years' experience of the biotechnology industry, including extensive first-hand knowledge of equity financing, business management and developing life science technology into commercial enterprises. Prior to her current role as CEO of ValiRx, she was a founder, director and CEO of Cronos Therapeutics Ltd. In her past roles, Dr Vainikka has developed and exited successful business models, negotiated corporate and academic transactions, and raised funding for a number of companies. Dr Satu Vainikka has gained valuable qualifications and awards with an MBA at Imperial College Business School in 2000, a PhD in signal transduction in oncology, University of Helsinki 1996, and a prestigious "EMBO" fellowship for post-doctoral research, at Imperial Cancer Research (Now CRUK).

Gerry Desler – Chief Financial Officer

Gerry is a qualified (1968) chartered accountant who rose to senior partner with a City accountancy firm, where he specialised in consultancy work, much of it involving funding and venture capital. He was involved in one of the first joint ventures in what was then the People's Republic of China in 1980. Gerry was previously the Finance Director of Premier Management Holdings plc, and is currently Company Secretary at Prospex Oil and Gas plc, and on the board of a number of private companies.

Dr George Morris – Chief Operation Officer

George has over 25 years' experience in biological and medical research. In the past he has worked at the medical departments of Guy's Hospital, King's College and University College, London. As a Research Scientist, he is an author of numerous books and peer-reviewed articles, approximately 70 abstracts, short reports and posters, and an inventor on multiple patents.

George was a founding member of the expert advisory panel, the 'Biotechnology and Finance Forum', set up jointly between the European Commission and the European Association of Securities Dealers. George was involved in a number of conferences and workshops with the EU research and agricultural directorates and is an 'expert' to the Commission, and has been invited into several policy discussion groups.

George has worked with a variety of commercial, governmental organisations and financial institutions in the US, Europe and Australia and many consultancy projects covering various biotechnology and financial activities. He is regularly asked to chair or participate in conferences, and acts as a 'Venture Academy' mentor. He has undertaken numerous continuing professional development courses covering finance and general management as well as in specific areas related to science & technology and statistics.

Kevin Alexander – Non-Executive Director

Kevin is a qualified solicitor in England and an attorney in New York and he was a partner at major law firms in both London and the United States for over 25 years. Since leaving the law he has been involved in forming and managing various businesses, both private and public. Kevin joined the Board in September 2006. He has an MA in law from Cambridge University.

Seppo Mäkinen – Non-Executive Director

Seppo Mäkinen has more than 25 years of senior advisory and executive experience in board level strategic, leadership and venture capital management in life sciences. He has particular expertise on medtech / diagnostics. His career includes 10 years as Director in Life Sciences at Sitra (Finnish Government Fund), followed by 13 years as co-founder and Managing Partner in Bio Fund Management Oy. Also, President of BioFund A/S, Copenhagen, which has EUR200m under management, and is one of the largest European VC funds investing in international life sciences. Key achievements include engineering exits such as the listing of six companies on international stock exchanges and completing over 10 trade sales transactions. Currently Seppo is Chairman and Board Member in four life science/healthcare companies and an advisor to Merieux Développement Fund.

Capital increases

Since it became listed on AIM in 2006, ValiRx has raised the equivalent of £22.8m of capital, including deferred considerations and milestones, through a series of 17 Placings over 10 years in order to get the company and its assets to where they are today.

There have been two share consolidations. In July 2007, there was a share re-organisation and consolidation on a 1-for-30 basis. This was followed by a 1-for-6 subdivision in February 2009 and, this was followed by a further 1-for-125 consolidation in April 2015. All numbers in the following summary table have been adjusted for these events.

The cash balance at the end of December 2016 was estimated to be £1.6m and a further £1.1m (net) was raised in a Placing of shares at 2.5p in March 2017, which will be sufficient to conclude the ongoing clinical trials for VAL201 and VAL401. However, clinical development is a capital intensive process and further funding will be required in the future to support additional trials and to advance VAL301 for endometriosis. Positive outcomes in the ongoing trials would be expected to trigger a significant valuation uplift.

Summary of capital raises

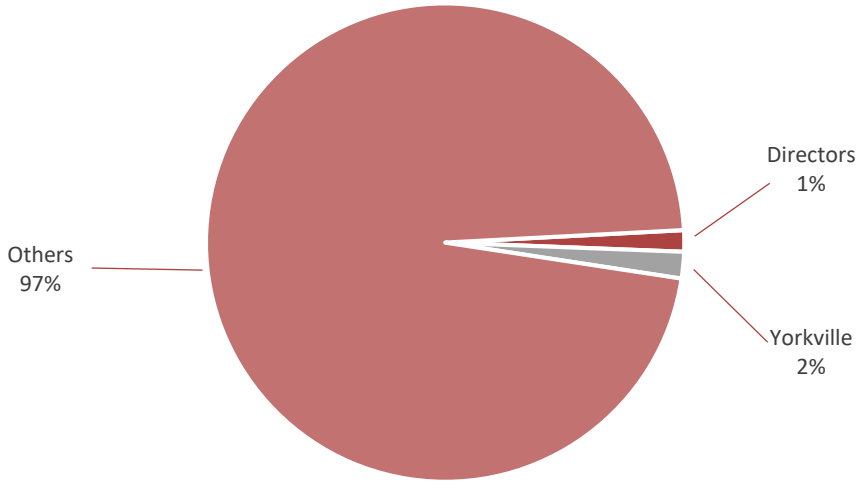
Comment	Date	Shares (m)	Price (p)	Raised (£000)	Shares o/s (m)	Valuation (£m)
Flotation on AIM	Oct-06	0.2	4,987.50	-	0.2	11.77
Placing @ £19.37 (15.5p)	Sep-07	0.0	1,937.50	311	0.3	4.89
Placing @ 750p	May-08	0.1	750.00	893	0.4	2.79
Acquisition of Cronos	Jul-08	0.1	750.00	690	0.9	3.48
Placing @ 125p	Mar-09	0.5	125.00	580	0.9	1.16
Placing @ 125p	Apr-09	0.2	125.00	199	1.1	1.36
Placing @ 150p	May-09	0.1	150.00	200	1.2	1.84
Placing @ 43.75p	Apr-10	1.4	43.75	625	2.7	1.18
Milestones to Cancer Research Technology	Oct-10	0.2	95.63	69	2.8	1.12
Placing @ 23.44p	Nov-10	1.1	23.44	255	3.9	0.92
Placing @ 75p	Feb-11	4.4	75.00	3,297	8.4	6.27
Acquisition of ValiFinn	Jan-12	0.1	65.00	78	8.5	5.51
Placing @ 56.25p	Apr-12	1.6	56.25	900	10.1	5.67
Placing @ 56.25p	Nov-12	3.6	56.25	2,032	13.7	7.70
Placing @ 40.63p	Nov-13	2.5	40.63	1,000	16.2	6.56
Placing @ 40.63p	Dec-13	7.2	40.63	2,932	23.4	9.49
Placing @ 25p	Dec-14	3.2	25.00	800	26.7	6.68
Placing @ 25p	Mar-15	3.2	25.00	800	29.9	7.48
Milestones to Cancer Research Technology	Jun-11	0.2	32.50	80	30.2	9.81
Subscription by Yorkville @ 30p	Sep-15	8.2	30.02	2,450	38.3	11.51
Placing @ 12.0p	Feb-16	4.2	12.00	502	42.5	5.10
Bracknor CLN conversions	Aug-16	13.9	7.20	1,000	56.4	3.44
Placing @ 6.0p	Sep-16	20.3	6.00	1,215	76.7	4.60
Yorkville CLN conversions	Dec-16	9.0	5.81	529	85.6	4.82
Placing @ 2.5p	Mar-17	46.5	2.50	1,163	132.2	3.30
Directors' subscription	Mar-17	1.2	2.50	30	133.4	3.30
Totals		**133.4**	**17.10**	**22,810**	**-**	**3.04**

The number of shares and share prices have been corrected for the 1-for-125 consolidation in April 2015 and the 1-for-30 consolidation in July 2007
Note: not every event is listed in this table
Source: Hardman & Co Life Sciences Research

Share capital

At the time of going to press there were 133,356,204 Ordinary shares of 0.01p each in issue and 3,734,900 outstanding share options (all out of the money).

ValiRx shareholders



Source: Company reports/announcements

Warrants

In addition, ValiRx has 83,480,011 warrants issued on the following basis:

- 15m 60 month warrants issued to Bracknor in 2016 – currently 4.5p*
- 2m 60 month warrants issued to Beaufort in 2016 at 6p
- 20m 24 month warrants issued to Beaufort investors in 2016 at 9p
- 46m 24 month warrants issued to Beaufort investors in 2017 at 5p**

** indicates approximate current exercise price pursuant to adjustment mechanism.*
*** to be issued following approval of the Special Resolution at 2017 AGM*

Convertible Loan Notes

- 12 month CLN's with 9% coupon issued in 2016 – ca.$1.9m (principal and accrued interest)

Potential fully diluted share capital

Ordinary shares in issue	133,356,204
Options	3,734,900
Warrants	83,480,011
Convertible loans ($1.9m capital & accrued interest) at 2.3p (est)	63,500,000
Fully diluted share capital	**284,071,115**

Source: Company reports; Hardman & Co Life Sciences Research

As indicated earlier in this report, ValiRx is undervalued by the market. In our opinion, the valuation of the company should be in the range of £20.9m (on a DCF basis) to as much as £251.5 (on an EV basis: average UK peers = £55.0m; average global peers = £251.5m). Based on 133.36m Ordinary shares is issue, this equates into a price per share of between 16p and 188p.

However, given that ValiRx has a number of options, warrants and convertible loan notes in existence, on a worst case scenario (unlikely) that all of these are exercised and/or converted, the fully-diluted share capital would be approximately 284m shares, which would place the valuation range at 7.4p to 88.5p. This still represents substantial share price appreciation if a valuation more in line with the fundamental asset value were to be achieved.

Share price performance

Source: Eikon Thomson Reuters

Risks

Investments in small early-stage pharmaceutical companies carry a significant risk and investors must be aware of this fact. In our opinion, the following risks are particularly relevant. Each of them could have an impact on time to reach market, cash flow breakeven and profitability.

Dilution risk

The company has sufficient cash to fund the ongoing trails of VAL201 and VAL401, but will need more capital to undertake further trials including bring VAL301 into a Phase I trial for endometriosis. There is no guarantee that the company will be successful in raising such funds, nor on the terms that such capital is raised, which could be dilutive to existing shareholders.

Commercialisation

The strategy of management is to out-licence its products for late-stage trials, regulatory submissions and commercialisation, and to receive an up-front on signature, milestones and royalties. The time taken to reach such agreements can be long and there is no guarantee that this would be on terms that are beneficial to shareholders. However, there is a willingness of big pharma to acquire novel assets especially when there is interesting supportive clinical data. The greater the level of clinical data, and hence de-risking, the more that commercial partners are willing to pay.

Patent robustness

As with all IP-rich companies, there is risk that the intellectual property is insufficiently covered by the global patents, allowing a competitor to gain market access. Any litigation could involve significant costs and uncertainties.

Regulatory

It is important for companies to liaise with regulators on a regular basis throughout the development programme. Any inadequacies could lead to regulatory action such as cessation of product development and loss of manufacturing or product licences.

Share liquidity

As with many small cap companies listed on AIM, there can be difficulty in buying and selling shares in volume. Market makers only guarantee prices in a very small number of shares.

Share register

The lack of deep-pocketed institutions on the share register is a significant risk. ValiRx will need more capital and support from HNWs can be limited, especially when significant capital losses have already been incurred.

Competition

The Company operates in a competitive field that attract much R&D investment, often dominated by large multinational players, most of which have significant financial resources to fund development programmes, marketing activities, etc.

Glossary

AR	Androgen Receptor
CNS	Central Nervous System
DCF	Discounted Cash Flow
ER	Oestrogen Receptor
GeneICE	Gene Inactivation by Chromatin Engineering
HDAC	Histone deacetylase
HSD10	Hydroxysteroid dehydrogenase type 10
NADH	Nicotinamide Adenine Dinucleotide Hydrogen
NSCLC	Non-Small Cell Lung Cancer
NPV	Net Present Value
MTD	maximum tolerated dose
MAD	maximum administrated dose
RECIST	Response Evaluation Criteria in Solid Tumours
RNAi	RNA interference (Ribonucleic acid)
PCWG2	Prostate Cancer Working Group 2: Guidelines on measuring prostate cancer progression and tumour response to treatment.
PSA	Prostate-specific antigen

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Notes

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Hardman & Co Research Limited (trading as Hardman & Co)
35 New Broad Street
London
EC2M 1NH
T +44 (0) 20 7194 7622

Follow us on Twitter @HardmanandCo

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Hardman Team

Management Team

+44 (0)20 7194 7622

John Holmes	jh@hardmanandco.com	+44 (0)20 7194 7629	Chairman
Keith Hiscock	kh@hardmanandco.com	+44 (0)20 7194 7630	CEO

Marketing / Investor Engagement

+44 (0)20 7194 7622

Richard Angus	ra@hardmanandco.com	+44 (0)20 7194 7635
Max Davey	md@hardmanandco.com	+44 (0)20 7194 7622
Antony Gifford	ag@hardmanandco.com	+44 (0)20 7194 7622
Ann Hall	ah@hardmanandco.com	+44 (0)20 7194 7622
Gavin Laidlaw	gl@hardmanandco.com	+44 (0)20 7194 7627
Vilma Pabilionyte	vp@hardmanandco.com	+44 (0)20 7194 7637

Analysts

+44 (0)20 7194 7622

Agriculture

Doug Hawkins	dh@hardmanandco.com
Yingheng Chen	yc@hardmanandco.com
Thomas Wigglesworth	tcw@hardmanandco.com

Bonds

Brian Moretta	bm@hardmanandco.com
Mark Thomas	mt@hardmanandco.com
Chris Magennis	cm@hardmanandco.com

Building & Construction

Tony Williams	tw@hardmanandco.com
Mike Foster	mf@hardmanandco.com

Consumer & Leisure

Mike Foster	mf@hardmanandco.com
Steve Clapham	sc@hardmanandco.com
Jason Streets	js@hardmanandco.com

Financials

Brian Moretta	bm@hardmanandco.com
Mark Thomas	mt@hardmanandco.com

Life Sciences

Martin Hall	mh@hardmanandco.com
Grégoire Pavé	gp@hardmanandco.com
Dorothea Hill	dmh@hardmanandco.com

Media

Derek Terrington	dt@hardmanandco.com

Mining

Paul Singer	if@hardmanandco.com

Oil & Gas

Angus McPhail	am@hardmanandco.com

Property

Mike Foster	mf@hardmanandco.com

Services

Mike Foster	mf@hardmanandco.com

Special Situations

Steve Clapham	sc@hardmanandco.com
Paul Singer	ps@hardmanandco.com

Tax Enhanced Services

Brian Moretta	bm@hardmanandco.com
Chris Magennis	cm@hardmanandco.com

Utilities

Nigel Hawkins	nh@hardmanandco.com

Hardman & Co

35 New Broad Street
London
EC2M 1NH
United Kingdom

Tel: +44(0)20 7194 7622

www.hardmanandco.com