ALIGN
RESEARCH

ValiRx

24th October 2018

Substantial value to be unlocked from leading clinical candidates as ValiRx progresses partnering/licensing discussions with several companies.

ValiRx is a drug development company with 4 therapeutic drugs in development. All have the potential to meet currently unmet medical needs & are targeting multi-billion dollar markets that are inadequately served by current drugs. The business model is focussed on progressing the clinical data of its therapeutic candidates & then concluding a partnering or an out-licensing deal.

VAL201 leads clinical developments

VAL201 is being developed for the treatment of androgen independent prostate cancer and hormone refractory prostate cancer. **Now nearing the end of Phase I/II trials the compound has demonstrated consistent high safety and tolerability and signs of efficacy throughout its clinical study.**

VAL401 on the cusp of Phase III trials

VAL401 has recently finished a Phase II trial as an oral treatment for late stage non-small cell lung cancer. Results showed the treatment had a statistically significant improvement in "Overall Survival" for patients with NSCLC compared to those receiving no treatment. **Detailed discussions are ongoing over a Phase III trial, with first dosing anticipated next year.**

Further long-term upside from pre-clinical candidates VAL101 & VAL301

VAL101 is a novel chemical entity, based on the company's proprietary GeneICE gene silencing platform, which has been in the selection and drug optimisation phase to block/silence the expression of a gene expressing Bcl-2 protein & which has been implicated and associated with various cancers. VAL301 is currently in late-stage pre-clinical development, initially as a non-invasive, effective treatment for the non-cancerous gynaecological condition endometriosis.

Risk weighted DCF valuation suggests potential upside of c.520%

Our total probability of success weighted NPV for VAL201 and VAL401 is £54.64 million, more than six times the current market cap. This equates to a target price of 10.28p. **Assuming successful approval for both drugs, the unrisked NPV rises to £115.16 million, suggesting c.13 times upside**. **We initiate coverage of ValiRx with a stance of Conviction Buy.**

This investment may not be suitable for your personal circumstances. If you are in any doubt as to its suitability you should seek professional advice. This note does not constitute advice and your capital is at risk. This is a marketing communication and cannot be considered independent research.

CONVICTION BUY – first target 10.28p

Valirx Bioscience Innovation

Key data

EPIC	VAL
Share price	1.65p
52 week high/low	7.625p/0.925p
Listing	AIM
Shares in issue	531,629,383
Market Cap	£8.8m
Sector	Biotechnology

12 month share price chart

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Corporate Background

Listing on AIM in October 2006 via the reverse takeover of Azure Holdings, ValiRx (VAL) is a biotechnology oncology focused company which specialises in developing novel treatments for cancer and associated biomarkers which enable the early detection of cancer and its therapeutic intervention.

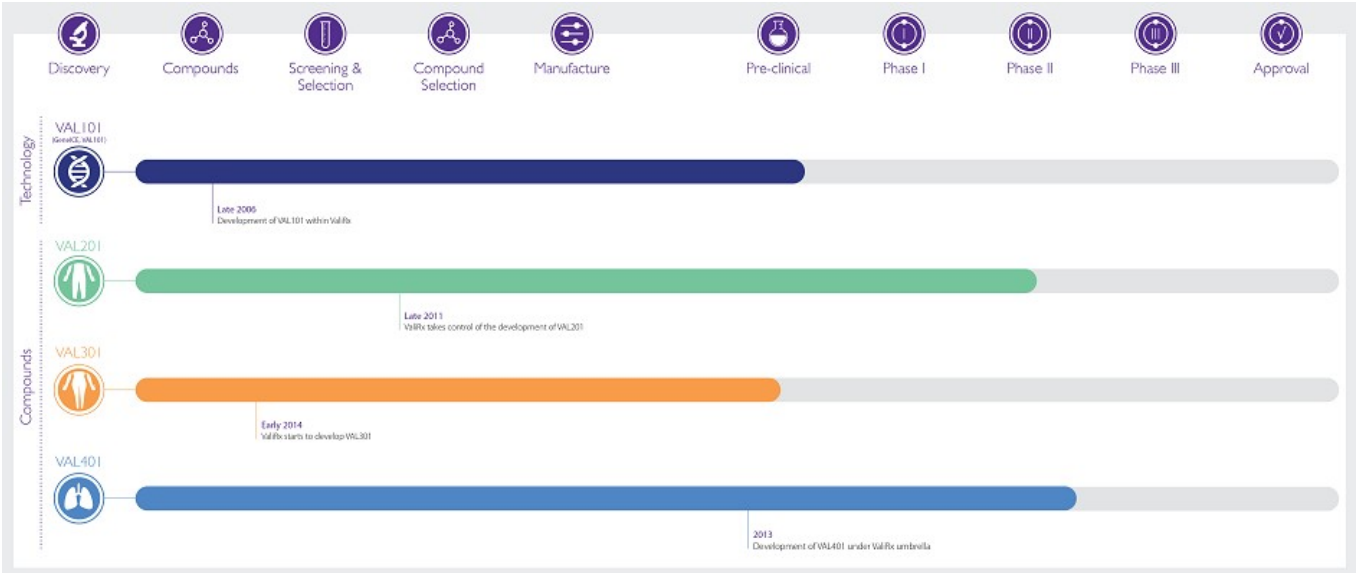
ValiRx's drugs and technology were acquired at a very early stage of their development from world-class institutions including Cancer Research and Imperial College and come with exclusive global commercialisation rights. The company today is focussing on delivering so called "target-based" agents, with novel mechanisms of action that selectively attack cancer cells, and hence, are less toxic than chemotherapy in improving a patient's quality of life and are more effective in improving current survival rates. **New drugs in this group, such as those in ValiRx's pipeline, promise to greatly improve outcomes for cancer patients.**

The company's business model is focussed on progressing the clinical data of its therapeutic candidates and then finding a partner or agreeing an out-licensing deal early in the development process. This approach aims for early-stage value creation and avoids the risks associated with full scale drug development. To minimise costs and focus on creating value from its portfolio, ValiRx has a "virtual" business model, outsourcing its pre-clinical and clinical development work to third-parties.

In order to finance its capital-intensive development activities ValiRx has completed a number of equity fundraisings during its time as a public company, agreed certain convertible loan facilities, received grants, and also with a modest amount of funds raised over the past year via the exercise of warrants. **A $3.25 million convertible loan agreement was agreed with Yorkville in September 2016 but there are now no obligations on either party following the final conversion of Yorkville shares in December 2017.**

Following the most recent placing in September this year a total of c.£29 million has been raised, with c. £25.3 million having been spent on product development and corporate costs as at 30th June 2018. ValiRx has a unique shareholder register for an AIM company, with it being made up mainly of private investors and the only one shareholder with a +3% holding.

ValiRx currently has four therapeutic drugs in development, all having the potential for meeting currently unmet medical needs, targeting multi-billion dollar markets that are inadequately served by current drugs, and having a number of worldwide patent filings and agreed commercial rights. They originate or derive from institutions including Cancer Research UK and Imperial College.



ValiRx pipeline. Source: Company

Clinical Development Candidates

VAL201

In July 2008 ValiRx entered into a license agreement with Cancer Research Technology Limited (CRTL) to evaluate a novel prostate cancer compound, VAL201. While the company owns the rights, certain milestone payments are due to CRTL. VAL201 is a peptide which is being developed for the treatment of androgen independent prostate cancer and hormone refractory prostate cancer.

Androgens are hormones, with the main types in the body being testosterone and dihydrotestosterone (DHT). Androgens have to bind to a protein in the prostate cell, called an androgen receptor, to work. They are required for normal growth and function of the prostate but also stimulate prostate cancer cells to grow by binding to and activating the androgen receptor and stimulating the expression of genes that cause prostate cells to grow. Hormone therapy, or androgen deprivation/suppression therapy, aims to reduce levels of androgens, to stop them from affecting prostate cancer cells.

VAL201 selectively prevents tumour growth by specifically inhibiting the proliferation of tumour cells. As a result, tumour growth is suppressed and metastasis is significantly reduced. It works by specifically targetting the association of an androgen receptor with Src, a protein that is important in tumour cell proliferation.

VAL201 is intended to target a specific pathway from the androgen receptor, treating the cancer without suppressing sexual and other functions and without other debilitating side effects many other therapies have. The VAL201 target is also associated with other cancers and there is significant potential for it to be used as a treatment for other hormone-induced cancers, such as breast and ovarian and also endometriosis (see VAL301 on page 11) as well as for preventive treatment.

In pre-clinical studies carried out in collaboration with the University of Oxford, VAL201 prevented cancerous growth in live models and treated models remained fertile and produced normal offspring. VAL201 may also have an effect in reducing bone metastasis, a common feature in advanced prostate cancer patients.

Current Phase I/II trials

VAL201 is currently in Phase I/II clinical trials for patients affected by hormone-sensitive and hormone-resistant (meaning that the cancer is no longer helped by any type of hormone therapy) prostate cancer at University College London Hospital (UCLH). This is a dose escalation study for up to 50 patients which is assessing the safety and tolerability of VAL201 in patients with locally advanced or metastatic prostate cancer and other advanced solid tumours. The primary outcome measures are to estimate the maximum tolerated dose and maximum administrated dose of VAL201 within an average timeframe of 18-26 weeks per subject. The secondary outcome measure is to evaluate the pharmacokinetics of VAL201, with other outcome measures focused on assessing anti-tumour activity.

The compound had a major trial review of its protocol at the end of 2017, which the regulatory authorities subsequently approved. This modification allowed ValiRx to escalate or accelerate the dosing regimen of the study, to a maximum of 16mg/kg of the drug administered, in several steps, if required. This escalation will see a substantial increase in the dose of VAL201 being administered to patients and allows treatment to more quickly reach its full therapeutic potential and potential anti-cancer impact on patients.

In September this year, ValiRx announced that the compound has demonstrated consistent high safety and tolerability and signs of efficacy throughout its clinical study.

Preliminary observations of the clinical data derived from the original dosing regimen has been completed regarding all the subjects that have been treated to date. These highlighted a dose-related impact on patients' physiology and chemistry, such as androgen PSA and various cell and protein turnover factors, which are important in the treatment of cancer. These are in line with anticipated outcomes as far as cancer reduction is concerned. The company continues to recruit appropriate patients for the concluding part of the trial, with completion expected in H1 2019.

Patent Protection

Country	Patent number	Date Filed	Granted/Allowed
United States	US 9919023	14 March 2008	Granted
Europe	EP 08717866.1	14 March 2008	Allowed
Japan	JP 2009-553162	14 March 2008	Granted
Australia	AU 2008228274	14 March 2008	Granted
United Kingdom	GB 1118831.5	01 November 2011	Granted
There are patent applications currently pending in many other territories and covering various aspects of the programme.			

Source: Company

Disease and market

According to Cancer Research UK, there were 47,151 new cases of prostate cancer in the UK in 2015, making it the second most common cancer in males. Worldwide, according to the World Cancer Research Fund, there are expected to be 1.3 million new cases in 2018.

In the UK, since the early 1990s, incidence rates have increased by more than two-fifths and around 4 in 10 prostate cancer cases are diagnosed at a late stage. There are around 11,500 prostate cancer deaths in the UK every year but survival has tripled in the last 40 years in the UK, with PSA tests (which measure the level of prostate-specific antigen (PSA) in the blood in men without symptoms of the disease) being a major factor in this. Survival rates are close to 100% when diagnosed at Stage I, falling to 30% when diagnosed at Stage IV.

VAL201 has a large potential market. According to a September 2018 report by Zion Market Research, the global prostate cancer therapeutics market was worth c.$10.1 billion in 2017 and is expected to grow to c.$17.2 billion by 2024, growing at a CAGR of 8% between 2018 and 2024.

Hormone therapy can be a life-long treatment for those with advanced prostate cancer. There are three main types: injections/implants, tablets or surgery (castration). All three aim to reduce the levels of hormones affecting the cancer cells, shrink the cancer and slow down its growth, even if it has metasised. While hormone therapy alone can't cure prostate cancer it can keep it under control, and is often combined with other treatments such as radiotherapy.

LHRH agonists (luteinizing hormone-releasing hormone agonists) are the most common type of injection/implant and reduce the production of testosterone in the body. Market leaders include AbbVie's Lupron, AstraZeneca's Zoladex and Watson Pharmaceuticals' Trelstar. GnRH antagonists (gonadotrophin-releasing hormone antagonists) are also used, including Ferring Pharmaceuticals' Firmagon. Tablets, or anti-androgens, work by binding to the androgen receptors so the androgens can't work. Drugs include Merck's Eulexin, AstraZeneca's Casodex and Astellas' Xtandi.

While the current trial is focused on patients with advanced prostate cancer, VAL201 could have a much wider application if the trial data continue to be positive, especially as a treatment during the so called "active surveillance" and "watchful waiting" periods of those with early stage disease (localised tumours).

VAL401

Under a joint-venture with SEEK group company Tangent Reprofiling Limited, named ValiSeek (55% owned by ValiRx), VAL401 has recently been trialled as an oral treatment for late stage non-small cell lung cancer in a Phase II Clinical Study in Tbilisi, Georgia, with first dosing of patients having commenced in October 2016 and the study completed in September 2017.

VAL401 is a reformulation of risperidone, a drug which was approved for sale in the US in 1993 and has a well-established safety record derived from clinical use in the treatment of schizophrenia and symptoms of bipolar disorder. The treatment has the potential to be administered alongside other chemotherapy or immunotherapy to provide anti-cancer activity alongside palliative and side effect mitigating quality of life improvements.

The reformulation activates anti-cancer activity, and this is the subject of granted US patents (see table below). A number of other US patents have been granted for VAL401, with one each in Australia and New Zealand, and international patents pending across Europe, Asia, Australasia and in North and South America, providing coverage in all significant markets worldwide.

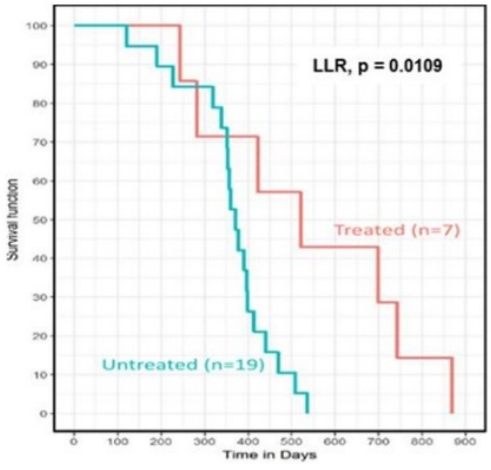
Phase II trial results

On 12th December 2017 shares in ValiRx more than doubled following news on the clinical progress of VAL401. Following up on the release of pharmacokinetic data from the completed Phase II trial, the company revealed that the VAL401 treatment had a statistically significant improvement in "Overall Survival" (OS) for patients with non-small cell lung cancer compared to those receiving no treatment.

For the trial, Stage IV Non-Small Cell Lung adenocarcinoma patients were recruited, having failed prior chemotherapy, with no further treatment options available. A total of eight patients received treatment with VAL401 for up to three months, with seven of these used for the Overall Survival data. For comparison, 20 case-matched patients who would have been eligible for the trial but did not consent in the same clinic, and who received palliative treatment only, were used, with 19 used for the survival calculation comparison. This group in effect set a benchmark as to how long patients would be expected to survive without the treatment.

Comparing the overall survival rates of treated patients to untreated patients and measuring from the date that patients received their first course of chemotherapy until the date of death, the data suggest that the VAL401 treatment provided a statistically significant improvement in survival.

The table below summarises the results and suggests that the patient for which the drug worked the best lived an extra year compared to the best case in the benchmark group. While only carried out on a small sample the data show a clear distinction in the survival time of treated patients compared to those who were not treated.



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

Further positive data on the results was released on 16th January 2018 following further analysis by data analytics company Ariana Pharma. **It confirmed that the VAL401 treatment has a measureable improvement on patient quality of life, in addition to a positive impact on the disease.**

The overall response to treatment rate in the "per protocol" population was 60%. This group excludes 2 patients who received treatment for less than 10 days, as well as one patient for whom the date of diagnosis is inconsistent. The "intention to treat" group includes all patients who completed screening, but excludes the one patient for whom the date of diagnosis is inconsistent.

The table below shows progression-free survival (PFS), defined as the length of time between initiation of VAL401 treatment and a patient's removal from the trial or death, and was considered as a comparison of responders to non-responders. In addition, in order to characterise responders to treatment, the definition of the Overall Survival was shortened to the length of time between the initiation of VAL401 treatment and death. **The mean values quoted represent an additional one month or longer of PFS and OS after response to VAL401 treatment.**

	PFS mean (range)	OS mean (range)
Responders (n=3)	8.7 weeks (7.1 - 11.6)	12.9 weeks (11.6 - 15.3)
Non-responders, intention to treat population (n=4)	2.5 weeks (0.4 - 4.7)	3.9 weeks (0.4 - 7.4)
Non-responders, per protocol population (n=2)	4.3 weeks (4.0 - 4.7)	7.1 weeks (6.8 - 7.4)

Quality of Life was measured at regular intervals during the trial via questionnaires, with 19 factors out of 28 improving from baseline to the end of the trial in several patients. Multiple patients reported an improvement in **pain, linked to high exposure to VAL401, with improvement in fatigue seen in lower exposures. What's more, responders and non-responders equally reported improvements in Quality of Life measures, suggesting palliative effects are in addition to survival benefit.**

Elsewhere, it was observed that the White Blood Cell Count (WBC), indicative of increased immune system activity, increased in 3 patients during the trial. Two of the responders were subject to a sustained increase in WBC, and one non-responder increased WBC on trial initiation before the WBC returned to baseline. **The increase suggests that VAL401 does not cause immune suppression, common in traditional chemotherapies, making it appropriate for considering the testing of VAL401 in co-administration with immuno-oncology treatment.** In addition, safety and tolerability was broadly comparable to other risperidone formulations. More detailed results have been published at https://clinicaltrials.gov/ct2/show/results/NCT02875340?cond=NCT02875340&rank=1&sect=X70156

A Phase III trial is now planned, with comparison to standard of care proposed in approximately 200 patients. This will be a randomised, controlled, multinational trial with the standard dosage proposed as 2 mg per day with patient dose adjustments after blood level analysis.

Since the results were released development has focussed on commercial areas. **Advanced conversations have continued with a number of prospective partners with the aim of achieving a partnership, to progress the project towards commercialistion**. Also, an advisory board of UK key opinion leaders has been consulted, addressing the significance of the results obtained and the positioning of VAL401 in the UK and global market. The panel included members of the patient advocate, hospital and consultant community, all having specialisms in oncology and particularly in end-of-life care in cancer patients.

In early September 2018 ValiRx provided an update on progress, stating that principal investigators have approved and signed the clinical study report and that the process of submission to and approval by the local ethics committees has commenced. Notification of receipt of the clinical study report was filed to the Ministry of Health in Tbilisi, before the end of July 2018, in accordance with regulatory expectations. **The company added detailed discussions are in progress over the Phase III clinical trial, with first dosing anticipated next year, subject to funding and partners external to the company having substantial input into the trial design.**

Patent protection

Country	Patent number	Date Filed	Date Granted/Allowed
United States	US 9072743	26 September 2013	07 July 2015
United States	US 9375433	08 May 2015	28 June 2016
United States	US 9585887	27 May 2015	07 March 2017
United States	US 9585890	31 May 2016	07 March 2017
United States	US9808462	27 February 2017	Allowed
Australia	AU 2013322612	26 September 2013	14 September 2017
New Zealand	NZ 706067	26 September 2013	01 November 2016

Disease and market

VAL401 is targeting a huge worldwide market, with non-small cell lung cancer (NSCLC) being the most common form of the disease, accounting for c.88% of all lung cancer according to LungHealth UK. The three types are adenocarcinoma, squamous cell carcinoma, and large cell carcinoma. The main treatments are surgery, chemotherapy, radiotherapy, chemoradiotherapy and symptom control treatment.

According to Cancer Research UK there were 46,388 new cases of lung cancer in the UK in 2015, making it the 3rd most common cancer, with 35,620 deaths in 2016. The World Health Organisation estimates 2.09 million new cases worldwide in 2018, with 1.76 million deaths. Smoking is the main risk factor, accounting for more than 80% of the total number of lung cancers.

Mortality rates for males and females combined decreased by 26% in the UK between 1971-1973 and 2014-2016. Incidence rates for males and females combined decreased by 8% in the UK between 1993-1995 and 2013-2015. However, there has been a marked difference between the sexes, with males seeing lower rates of incidence and deaths and females higher. More people with a known stage are diagnosed at a late stage (72-76% at stage III or IV), than an early stage (24-28% at stage I or II). Prognosis can be poor at all stages compared to other types of cancer, with the five year UK survival rate being 35% at stage I and just 6% at stage III for all adults during 2003-2006.

This is a large but crowded market, with many approved drugs available, but one which still has a large unmet need due to the high incidence and low survival rates. Current market leaders including Roche's Avastin, Eli Lilly's Alimta and Novartis' Afinitor. In addition, according to the National Cancer Institute, there are currently 485 open trials examining non-small cell lung cancer. **According to a March 2017 report from Grand View Research, the global non-small cell lung cancer therapeutics market is expected to reach a value of $12.2 billion by 2025.**

Pre-Clinical Development Candidates

VAL101

VAL101 is a novel therapeutic based on the company's proprietary GeneICE (Gene Inactivation by chromatin engineering) gene silencing platform. The GeneICE technology platform, based on natural mechanisms, enables the design of compounds for the selective "silencing" of so called "rebellious genes". These are genes which are overexpressed or are erroneously expressed when they should not be, causing problems such as cancer and potentially some neurological problems. It works by recruiting and applying gene silencing complexes known as Histone Deacetylase Complexes (HDACs) to target genes involved in cancer to effectively switch them off and potentially inhibit tumour growth.

ValiRx has a world-wide exclusive licence from Imperial College for the GeneICE technology and for any resulting products, in addition to newly generated intellectual property rights. To date the company has attracted two Eurostars grants for GeneICE. The first grant of €1.4 million was to further develop the GeneICE platform. The second grant for up to €1.6 million was to progress the pre-clinical studies of VAL101 and to build the associated cancer models. Patents for GeneICE have been granted in Europe, US and Australia

Recent work has seen VAL101 in the target selection and drug optimisation phase to block/silence the expression of a gene expressing Bcl-2 protein which has been implicated and associated with various cancers, including pancreatic cancer.

In September 2017 the company announced an update on work to generate a commercially viable molecular structure for VAL101. Pre-clinical studies of the first generation showed that, while the molecule worked, Bcl-2 was seen to reduce and that cancer cell death occurred, the molecule's structure and manufacture required optimisation for commercial production. Preliminary results of an optimised, commercially viable second generation of the VAL101 molecule demonstrated gene silencing levels that were similar to the original structure.

Then in April 2018 the company announced that further work on the optimised molecule had shown a superior apoptotic (programmed cell death) effect in comparison to currently available reagents. This will be the compound that will be taken forward for preparation and use in clinical trials.

ValiRx intends to accelerate VAL101's late pre-clinical studies in preparation for the compound's entry into the clinic. The company is working in partnership with commercial and academic collaborators Deutsche Krebsforschungzentrum, the Institute of Oncology in Heidelberg and Pharmatest Services Limited in Finland to progress the pre-clinical studies, and adding further commercial partners in the US and China, in order to support manufacturing and clinical development.

VAL301

VAL301, a reformulation of VAL201, is currently in late-stage pre-clinical development, initially as a non-invasive, effective treatment for the non-cancerous gynaecological condition endometriosis. Pre-clinical work on VAL201 highlighted the compound's specific mode of action has the potential to protect uterine tissue from the oestrogenic (hormonally-induced) effects that give rise to endometriosis, with minimal impact on bone density or fertility, major drawbacks frequently encountered with the current commonly used drugs. **Having the same active pharmaceutical ingredient as VAL201, the development of VAL301 is likely to benefit from progress being seen in the VAL201 Phase I/II clinical trial.**

Initial in-vitro results from a pre-clinical study showed up to a 50% reduction in endometrial lesion size directly related to dosage and two generations of offspring produced by treated animals. **This strongly suggests that the peptide does not affect fertility the same way other treatments for endometriosis do**. Also, a pre-clinical study in an animal model has indicated that VAL301 is unlikely to affect bone density, another unwanted side effect often reported with hormone therapies. These findings suggest an important step in the development of precision medicine for a complex disease that has to date been very difficult to classify and predict.

In July 2018, the US patent and trademark office granted a US Patent for VAL301 entitled *"Inhibitors of the interaction between a src family kinase and an androgen receptor of estradiol receptor for the treatment of endometrioses".* **Final laboratory tests are currently underway, with ValiRx focusing on arriving at the optimal formulation, prior to advancing VAL301 into additional toxicology trials and then clinical trials within the next twelve months dependent on funding and regulatory clearance.**

Disease and Market

Endometriosis is a common condition where tissue that behaves like the lining of the womb (endometrium) is found in other parts of the body, generally the fallopian tubes, ovaries and tissue around the uterus. It mainly affects girls and women of childbearing age, can be a debilitating condition and it represents one of the major causes of female infertility.

According to a 2009 study (*Priorities for endometriosis research: recommendations from an international consensus workshop: Rogers PA, D'Hooghe TM, Fazleabas A, et al*), 1 in 10 women of reproductive age in the UK suffer from endometriosis and 10% of women worldwide (c.176 million) have the condition. Symptoms can include inflammation, severe cramps, heavy and prolonged menstrual flow, nausea and vomiting, chronic fatigue, long-term pelvic pain and infertility.

Because there is no known cause of endometriosis, and because the development of the condition is poorly understood, there are no known ways to cure or prevent it. Instead, the only treatments currently available are pain management via pain killers, surgery or hormonal treatments, which are known to have side-effects. VAL301 therefore offers a potentially effective treatment.

AbbVie's Lupron is currently the top selling drug for endometriosis symptoms. A composition patent is set to expire in 2019, opening the door for generics. However, in July 2018, in co-operation with NASDAQ listed Neurocrine Biosciences, AbbVie received FDA approval for ORILISSA™ (elagolix), the first and only oral gonadotropin-releasing hormone (GnRH) antagonist specifically developed for women with moderate to severe endometriosis pain.

According to analysts at GlobalData, the endometriosis market, across the key geographies of the US, France, Germany, Italy, Spain, the UK and Japan, is set to rise from around $1.72 billion in 2015 to just over $2 billion by 2025.

Financials

2017 results

For the year to 31st December 2017 ValiRx saw net losses fall from £4.75 million to £3.02 million following a decrease in clinical trial expenditure on medicinal products - the manufacturing costs for VAL201 and VAL401 incurred for their respective trials were borne during 2016. R&D costs fell from £2.38 million to £1.75 million, with admin expenses down from £1.79 million to £1.47 million.

The net cash outflow from operations for the year was reduced to £2.35 million following the receipt of £0.64 million of tax credits. Four separate placings during the period raised a net total of £3.07 million, with £0.26 coming in from convertible loan notes. That left cash at the period end at £0.7 million, up from £0.56 million 12 months previously. In December 2017, ValiRx announced the final conversion of the convertible loan note agreement with Yorkville, with there being no further obligations for either party.

Interims

For the six months to 30th June 2018 the net loss rose marginally, by 6.4% to £1.91 million. This was after an 18% rise in R&D costs to £0.85 million and a 21% rise in admin expenses to £0.92 million. There was a net cash outflow of £1.86 million in the first half, down from £0.85 million in H1 2017, with £2.07 million raised in total via equity issues. Cash was £0.59 million at the period end and all debt was eliminated following the conversion of the Yorkville loan.

The most recent fundraise was announced on 14th September, with ValiRx raising £1.15 million gross through a placing of 76,666,666 new ordinary shares at a price of 1.5p each. The net proceeds will be used to extend and expand the scope of the VAL201 clinical trial and to progress the development of the pre-clinical VAL301 and VAL101 programmes and towards clinical trials. Also in September, ValiRx received R&D Tax Credits amounting to c.£416,000.

ValiRx had a total of c.93.6 million warrants outstanding as at the date of this report, exercisable at prices between 4.25p and 9p, with those issued to previous convertible loan provider Bracknor Fund Ltd being adjustable. Prior to Feb 2018 there were 3,793,400 share options in existence, but with a minimum exercise price of 43.125p are all out of the money at the current share price. This was prior to the issuance of a total 34.6 million new options to the directors in February, exercisable at a price of 4p per share at any time up until 7th February 2028.

Management

Oliver de Giorgio-Miller - Chairman

Oliver has a wealth of experience in the management and commercial advancement of life science companies. He has worked for over 30 years with several global pharmaceutical and medical device companies including Schering AG, Hoffman la Roche, Intavent-Orthofix and Photo Therapeutics, a Cancer Research UK company and he has extensive experience advising a number of other 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 experience 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 Limited.

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 the following qualifications and awards: MBA at Imperial College Business School 2000, PHD in signal transduction in oncology, University of Helsinki 1996, "EMBO" fellowship for Postdoctoral research, at Imperial Cancer Research.

Dr. George Morris - Chief Operations Officer

George has over 25 years' experience in biological and medical research, and financial services. In the past he has worked for Guy's hospital medical school department of medicine, King's College and University College London. As a Research Scientist, he is an author of numerous books and articles on refereed papers, approximately 70 abstracts, short reports and posters, and an inventor of 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 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 in his areas of experience, including acting as a 'Venture Academy' mentor. Has undertaken numerous continuing professional development courses covering finance and general management as well as in specific areas related to science & technology, statistics.

Gerry Desler - Chief Financial Officer

Gerry is a chartered accountant, who qualified in 1968 with a City firm, before becoming a partner in 1970. Between 1985 and 1990 he was the Senior Partner. During his time in the City, he has 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, an AIM listed company and is on the board of a number of private companies. Gerry also holds positions as Company Secretary at Prospex Oil and Gas Plc both Aim listed companies. (Member of Audit Committee)

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 is a director of Valirx Plc, and joined the board in September 2006. He has an MA in law from Cambridge University.

Key Risks

General biotechnology industry risks

ValiRx faces all of the typical risks involved in the research and development of new drugs, including costs of product development, long lead times to market, potentially unsuccessful results from clinical trials, designing trials appropriately, a strict regulatory environment and a reliance on third parties. The risks are mitigated somewhat by the company having four candidates in development, all of which target different diseases.

Stage of candidate development

While ValiRx's two clinical candidates and two pre-clinical candidates have delivered encouraging results so far, there is no guarantee that positive results can be repeated in further clinical trials and that expected timeframes can be met. The development of clinical products for new medical treatments is inherently uncertain, with high failure rates in clinical studies for both early and late-stage development products. Products can frequently run into unforeseen issues of safety and efficacy upon entering clinical trials in human subjects and more substantial Phase III trials can fail to repeat findings of earlier studies on a larger scale.

Funding risk

ValiRx has mainly funded its operations via a series of equity fundraisings since its formation. No revenues from product sales are currently being earned and it may be several years before revenues are earned from its product candidates. While the company has raised capital to support its development activities, assuming that the candidates advance further, additional capital will need to be raised.

Competition/commercial risk

While the markets which ValiRx is targeting are large, they are all rapidly evolving and contain a number of well-funded "big-pharma" competitors with products that have been approved for market. It is possible that even if ValiRx's products are eventually approved for sale they may not capture a significantly large enough share of the market to be economic and that developments by competitors may make the products obsolete. ValiRx plans to mitigate the commercial risk by finding a partner or agreeing an out-licensing deal early in the development process.

Intellectual property risk

Successfully commercialisation partly depends on the company's ability to obtain and maintain protection for its intellectual property so it can stop others from copying its products. There is also the risk that the intellectual property is insufficiently covered by the patents granted. Mitigating this risk, ValiRx invests in maintaining and protecting its intellectual property, with the company having a wide IP portfolio which covers all major areas worldwide for VAL201 and VAL401 in addition to other patents for VAL301 and GenelICE.

Valuation

Discount Cash Flow

To highlight the potential value offered from the VAL201 and VAL401 candidates we have prepared a ten-year discount cash flow analysis of each product, in both the US and European markets, using a range of assumptions. We apply no value to VAL101 and VAL301 at their current stage of development.

Assumptions

	VAL401	VAL201
Year on sale	2025	2025
Price per patient per annum (£)	21,000	2,820
New cancer cases rate of change US	-1.4%	-3.0%
New cancer cases rate of change Europe	-1.8%	0.0%
NSCLC rate	88%	N/A
Rate diagnosed at late stage	75%	40%
Royalty	10%	10%
Discount rate	12%	12%
Probability of success	49.56%	15.21%

Our model assumes that both products will reach market in 2025, capturing 1% of the market in the first year and then a further 1% every year to reach 10% in 2034. Patient numbers have been assumed using the latest figures from the National Cancer Institute in the US and Eurostat in Europe, growing in line with historic trends, adjusted for population growth. At this stage, only advanced patients of both non-small cell lung cancer and prostate cancer are assumed to be potential users of the drugs.

In terms of pricing we assume that VAL401 will attract a similar annual price to Avastin (£21,000) and VAL201 will cost the equivalent of Zoladex (£235 a month). ValiRx is assumed to earn royalties of 10% on sales. **Crucially, we assume that a partner is found and will fully fund the Phase III trials of both candidates to completion.** Offsetting this and also due to uncertainty over any potential deal, we also forecast no developmental or commercial milestone payments during the period of the DCF analysis. **This is highly conservative as, demonstrated in the industry deals section below, milestone payments from out-licensing can run into the hundreds of millions of dollars.**

To derive the final value we discount back the cashflows at a rate of 12% and then adjust for probability of success using figures from the Biotechnology Innovation Organization's *Clinical Development Success Rates 2006*-2015 report.

With VAL401 being on the cusp of Phase III trials (albeit with financing to be found), we adjust its cashflows by a 49.56% probability of success, for a total NPV of **£53.56 million.** We apply a probability of success of 15.21% to VAL201 given that Phase I/II trials are ongoing, for an NPV of **£1.08 million. While this figure is markedly lower than VAL401 at this point, mainly due to the lower predicted sales price and lower probability of success, there is significant upside potential should VAL201 be applied earlier in the prostate cancer treatment timeline.**

Therefore, our base case total probability of success weighted NPV for VAL201 and VAL401 is £54.64 million, or 10.28p per share.

Peer Analysis

While drug development companies differ markedly between number of candidates, stage of development and indication, it is worth looking at ValiRx's valuation in comparison to its London listed peers. In the table below we identify a selection of such drug development companies with oncology focused candidates, valued at below £100 million. For a cleaner comparison, we eliminate several companies from the analysis which have recently suffered from poor trial results (i.e. ImmuPharma and Faron Pharmaceuticals) or announced a corporate transaction (Midatech Pharma).

Company	EPIC	M. Cap. (£m)	EV (£m)	Cash (£m)*	Historic annual burn rate (£m)	Cash to burn rate	Stage of development
ValiRx	VAL	8.8	7.05	1.75[1]	3.2	0.55	Phase 2
Redx Pharma	REDX	9.5	-0.8	10.3	10.15	1.01	Phase 1/2a
Hemogenyx Pharmaceuticals	HEMO	9.9	8.7	1.2	0.78	1.54	Pre-clinical
Nuformix	NFX	10.8	10.5	0.3	0.73	0.41	Phase 1
Evgen Pharma	EVG	14.2	10.6	3.6	2.91	1.24	Phase 2
Sareum	SAR	22.0	20.6	1.38	1.71	0.81	Phase 2
Scancell	SCLP	37.8	27.5	10.3	4.94	2.09	Phase 2
Silence Therapeutics	SLN	84.2	50.0	34.2	14.4	2.38	Phase 3

** as at last balance sheet date*

[1] including £1.15m placing proceeds post period end

Results of the analysis show that ValiRx commands the lowest market capitalisation of all of the peer group and the second lowest enterprise value, suggesting that it is being undervalued.

An explanation of this may be that compared to its peers ValiRx has the lowest cash "runway" considering its historic spending. We calculate annual burn rate by looking at total R&D and admin expenses in the previous financial year. On this basis ValiRx, considering cash as at 30th June 2018 plus the recent £1.15 million placing proceeds, has just over six months' worth of cash left. What is clear is that further funds will need to be raised, either from a partner or the equity/debt markets, before VAL401 is able to enter into its planned Phase III trial.

Industry deals

Given the clinical progress made with VAL201 and VAL401 and the company's approach to out-licensing, we believe that ValiRx should be close to agreeing a deal with potential commercial partners in the form of big pharma companies. To illustrate the potential value here, many recent deals for Phase II therapeutic candidates have run into the many hundreds of millions of dollars, representing many multiples of ValiRx's current market cap.

According to IQVIA's *Pharma Deals Half-Year Review of 2018* oncology continues to be the principal therapy area for deals in the life sciences sector, with 33% of deals signed in H1 2018 involving oncology.

While not perfect comparators, we highlight a number of oncology deals which have been completed in the past year or so below. To indicate the kind of value the company could unlock should a deal be done for VAL 201 or VAL401, all below agreements were signed at a similar stage of development as ValiRx's lead candidates.

Endocyte/ABX

In October 2017, **Endocyte, Inc. (NASDAQ:ECYT),** agreed an exclusive worldwide license for PSMA-617 from **ABX GmbH**. This was prior to moving into Phase III trials of 177Lu-PSMA-617 earlier this year. 177Lu-PSMA-617 is a radioligand therapeutic (RLT) that targets the prostate-specific membrane antigen (PSMA), present in approximately 80% of patients with metastatic castration-resistant prostate cancer.

Endocyte made an upfront payment of **$12 million** to ABX, issued 2 million of its shares to ABX (worth c.**$2.8 million** at the time) and issued a warrant for the purchase of up to 4 million additional shares. ABX is eligible for regulatory and commercial milestones of up to **$160 million**, and tiered royalties beginning in the mid-teens.

ArQule/Basilea

In April 2018 **ArQule Inc. (NASDAQ: ARQL)** announced a license agreement with **Basilea Pharmaceutica Ltd. (SIX: BSLN)** for oncology drug candidate ARQ 087 (derazantinib), which targets the fibroblast growth factor receptor (FGFR) family of kinases. The exclusive license is worldwide, excluding the People's Republic of China, Hong Kong, Macau and Taiwan. The drug has demonstrated favorable clinical data in a biomarker-driven Phase 1/2 study in bile duct cancer patients and is recruiting for a Phase III trial.

Under the deal ArQule received an upfront payment of **$10 million** and is eligible for up to **$326 million** in regulatory and commercial milestones. ArQule is also entitled to receive staggered single-digit to double-digit royalties on net sales upon commercialisation. Basilea will be responsible for all costs and expenses of development, manufacture and commercialization in its territory. Under certain circumstances, ArQule may have the opportunity to promote derazantinib in the US directly.

Mologen/Oncologie

Also in April, **Mologen (Frankfurt: MGN)** announced the signing of a license deal for the Chinese territory and a global co-development agreement with **Oncologie Inc.** for its lead compound lefitolimod, which is currently being developed within the framework of a pivotal study for first line maintenance therapy for colorectal cancer. Key data of its phase II IMPULSE study in small cell lung cancer were announced in April 2017. The agreement includes the development, manufacture and commercialization of lefitolimod in China and a planned global co-development program.

Mologen received an initial payment of **€3 million**, with a **€2 million** equity investment, due within 12 months. Development and commercialisation milestones can amount to above **€100 million** and will be paid over several years. Additionally, Mologen will receive low double digit royalties on sales.

Can-Fite/CMS

In August 2018 **Can-Fite BioPharma (NYSE:CANF)** announced it had signed a license, collaboration and distribution agreement with **CMS Medical Venture Investment** for the commercialisation of Can-Fite's Piclidenoson for the treatment of rheumatoid arthritis and psoriasis and Namodenoson for the treatment of advanced liver cancer and non-alcoholic fatty liver disease/Non-alcoholic steatohepatitis (NAFLD/NASH) in China (including Hong Kong, Macao and Taiwan). Phase II studies with Namodenoson for the treatment of advanced liver cancer and NAFLD/NASH are ongoing, with patients being enrolled for a Phase III trial of Piclidenoson for the treatment of rheumatoid arthritis and plans to shortly initiate patient enrollment for its Phase III trial of Piclidenoson for the treatment of psoriasis.

Under the deal, CMS Medical made an upfront payment of **$2 million** and will make milestone payments of up to **$14 million** upon the achievement of certain regulatory milestones and payments of up to **$58.5 million** upon the achievement of certain sales milestones. In addition, the agreement provides for double-digit royalty payments on net sales.

Conclusion

ValiRx is making good progress in the clinic with its two lead candidates. The signing of a value enhancing deal with a development/commercial partner for VAL401 particularly, but also for VAL201, looks not far off, as has been flagged by the company in recent RNSs. We believe that given the current late stage of 401 in Phase III trials and the very real likelihood of a partnership deal on the near horizon that the current post recent placing price of sub 2p provides an excellent opportunity to enter into the stock in anticipation of such catalysts and that a re-rating to a realistic level is now overdue. **As has been evidenced before on positive trial RNSs, such news we believe would trigger a large rise in the share price**. Additionally, as well as cementing value within the development portfolio, we would expect that any such partnership deal would include a funding element as well as attract institutional investment, thus reducing the market's concerns over this major risk to the investment case and putting ValiRx into a higher league.

As discussed, our total probability of success weighted NPV for VAL201 and VAL401 is £54.64 million, more than six times the current market cap. We use this to set our initial target price of **10.28p per share**. As ValiRx moves along the valuation curve we expect to reduce our discount rate and increase the probability of success rate, thereby providing further upside potential. We point out that, assuming successful approval for both drugs, the unrisked NPV (100% probability of success) rises to £115.16 million, suggesting c.13 times upside. **Accordingly, we initiate coverage of ValiRx with a stance of Conviction Buy.**

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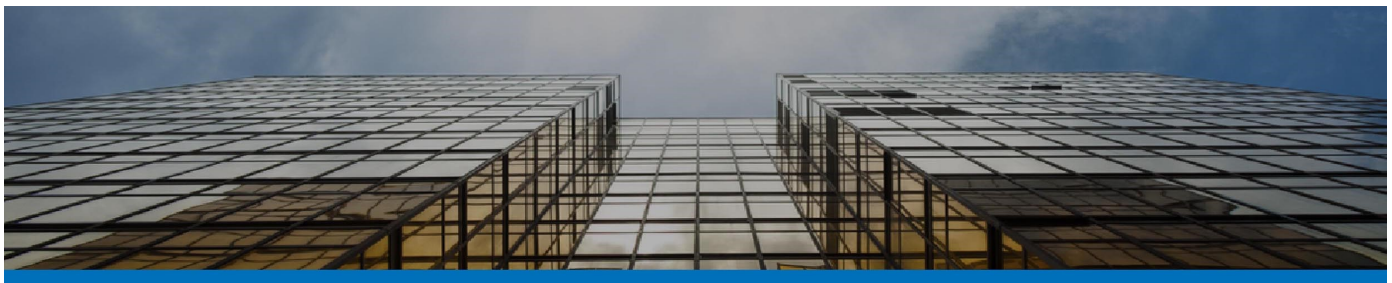

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