hardman&co

Verona Pharma

De-risking of RPL554 continues

VRP is developing first-in-class drugs that treat unmet medical needs in respiratory disease. RPL554 is being fast-tracked to commercialisation by focusing on a $3.2bn market segment poorly serviced by existing drugs. Four out of five trials in the clinical development programme have been completed with positive outcomes, with the fifth due to report in 2Q'16. To date, RPL554 has been shown to have a strong bronchodilatory effect with minimal side effects and will certainly be attracting the attention of drug majors. Median prices paid for Phase II respiratory assets have headline valuations of $285m (£190m), equivalent to 19p per share.

- **RPL554 in asthma:** VRP has reported positive outcomes from a Phase IIa trial of nebulised RPL554 in 29 mild-to-moderate asthma patients which commenced in June 2015 and was fully recruited by early November 2015. This complex cross-over study compared RPL554 with two doses of salbutamol, or placebo.

- **Outcome:** The bronchodilatory effect of RPL554 was equivalent to that seen with the highest dose of nebulised salbutamol used to treat an asthma attack. No GI side effects or CV effects of concern were observed. These results suggest that RPL554 could be a useful addition for treating respiratory disease.

- **Results:** A more complete data set will be presented at a respiratory conference in May, by which time, Verona is also likely to have released data from its Phase IIa trial in COPD patients to identify if RPL554 has an additive broncholdilatory effect. These trials are all contributing significantly to the de-risking of RPL554.

- **Valuation:** About £18m has been invested in R&D to get VRP where it is today, compared to an EV of £34m. This positive outcome, coupled with the potential Phase IIa results in COPD, represents a major value inflection point and will progress the interest of the drug majors towards a commercial licensing deal.

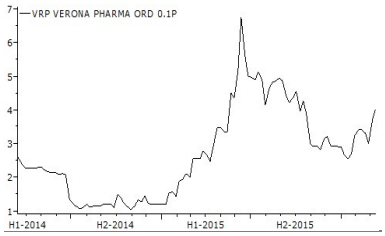
- **Investment summary:** Historically, efficacy of PDE inhibitors has been positive, but putative drugs have failed due to side effects. To date, results with the new formulation of RPL554 have exceeded expectations, which augurs well for the pivotal Phase IIb trial due to start in early 2017. With big pharma constantly searching for new respiratory assets, RPL554 will definitely be on the radar.

Financial summary and valuation

Year end Dec (£000)	2012	2013	2014	2015E	2016E	2017E
Sales	0	0	0	0	0	0
Royalties	0	0	0	0	0	0
Underlying EBIT	-2,585	-2,630	-3,601	-8,585	-4,164	-4,418
Reported EBIT	-2,653	-2,817	-3,793	-9,102	-4,556	-4,831
Underlying PBT	-2,565	-2,627	-3,571	-8,543	-4,160	-4,491
Statutory PBT	-2,633	-2,814	-3,763	-9,060	-4,552	-4,902
Underlying EPS (p)	-0.8	-0.7	-0.3	-0.7	-0.3	-0.4
Statutory EPS (p)	-0.8	-0.7	-0.3	-0.8	-0.3	-0.4
Net (debt)/cash	961	604	9,970	2,188	-1,193	-4,579
Capital increase	1,002	1,802	13,103	100	100	100
P/E (x)	-	-	-	-	-	-
EV/sales (x)	-	-	-	-	-	-

Source: Hardman & Co Life Sciences Research

Pharmaceuticals & Biotech



Source: Fidessa

Market data

EPIC/TKR	VRP
Price (p)	4.0
12m High (p)	6.2
12m Low (p)	1.0
Shares (m)	1009.9
Mkt Cap (£m)	40.4
EV (£m)	34.3
Free Float*	58%
Market	AIM

**As defined by AIM Rule 26*

Description

Verona Pharma plc is a UK-based biopharmaceutical company focused on development of innovative prescription drugs to treat respiratory diseases with significant unmet medical needs, such as COPD, asthma & cystic fibrosis

Company information

CEO	Jan-Anders Karlsson
CFO	Biresh Roy
Chairman	David Ebsworth
	0203 283 4200
	www.veronapharma.com

Key shareholders

Directors	2.9%
Arthurian	20.8%
Aviva	18.0%
Fidelity	7.6%
Vivo Capital	6.4%

Next event

11 June	AGM
2Q'16	RPL554 COPD Ph.IIa
Sept	Interims
4Q'16	RPL554+SoC combo

Analysts

Martin Hall	020 7148 1433
	mh@hardmanandco.com
Gregoire Pave	020 7148 1434
	gp@hardmanandco.com

RPL554 trial update

Half way through three year trial programme with RPL554

Verona is in the middle of an important three-year clinical development programme for RPL554 in respiratory disease. Having initially established that the drug was efficacious in a small proof-of-concept Phase II clinical trial using a formulation that was not commercially viable, this programme has been designed to replicate and enhance those initial findings with a commercial formulation of RPL554 delivered via a nebuliser. To date, four trials from the committed five trial programme have been completed with successful outcomes. Data reported from these trials are important when designing the protocol for the pivotal Phase IIb study in COPD patients which would likely start in early 2017, and for which further funding/partnering will be required.

Safety & tolerability studies

Trial results in 2015 showed that RPL554 was safe and well tolerated

The clinical trials undertaken during 2015 were largely early stage (Phase I) studies to assess the safety, tolerability and pharmacokinetics of the new formulation of RPL554, initially in healthy male volunteers and then progressing to patients with stable COPD. Overall, the results greatly exceeded expectations. Patients were found to tolerate much higher doses of the new formulation of RPL554 without evidence of side effects. At these higher doses, a more profound bronchodilatory effect was observed which was associated with an improvement in lung function. Pharmacokinetic data suggested that RPL554 would be well-suited to a twice daily dosing regimen that would improve patient convenience and compliance.

RPL554 development programme

Trial	Phase	Patients	Aim	Status
SAD*	Phase I	Healthy male volunteers	To assess the safety, tolerability and pharmacokinetics of RPL554, with the secondary aim of ascertaining the maximum tolerated dose (MTD)	✓
MAD*	Phase I	Healthy male volunteers	To assess the safety, tolerability and pharmacokinetics of 5½ days of RPL554	✓
MAD*	Phase IIa	Stable COPD	To assess the safety, tolerability and pharmacokinetics of 5½ days of RPL554 in patients with COPD	✓
Asthma	Phase IIa	Mild-to-moderate asthma	To assess single dose nebulised RPL554 versus two doses of salbutamol or placebo in 29 mild-to-moderate asthmatics	✓
COPD	Phase IIa	COPD	To assess nebulised RPL554 versus placebo in addition to standard of care bronchodilators to identify whether RPL554 produces an additive bronchodilatory effect	2Q'16
COPD	Phase IIb	COPD	Pivotal placebo-controlled trial to confirm improved lung function and reduced symptoms, together with secondary benefits regarding hospital stays and readmission rates	2017

SAD: Single ascending dose
MAD: Multiple ascending doses
**The SAD/MAD trial was a single trial performed in three stages*
Source: Company reports; Hardman & Co Life Sciences Research

Pivotal phase IIb study in COPD due to commence in 2017....

...when funding/licensing has been arranged

Phase IIa in asthma

High dose RPL554 produced a similar bronchodilatory response to that seen with the highest dose of salbutamol...

Today's results are from a Phase IIa clinical trial in 29 mild-to-moderate asthma patients which commenced in June 2015 and was fully recruited by early November 2015. In this cross-over study, patients received a single dose of nebulised RPL554, two doses (2.5mg and 7.5mg) of nebulised salbutamol, or placebo. The full data set will be reported at a respiratory conference in May 2016.

...but with a better side effect profile

- Dose-dependent (0.4-24.0mg) bronchodilatory response seen with RPL554; the effect with 24mg RPL554 was comparable to that seen with the highest dose (7.5mg) of salbutamol used to treat exacerbations in the emergency department
- RPL554 did not elicit any serious adverse events at any dose and was well tolerated

This study had a complex design, employing a seven-way cross-over, but met its primary end-point, with RPL554 demonstrating a dose-dependent bronchodiolatory effect in asthma patients. The highest dose (24mg) of nebulised RPL554 produced the same bronchodilatory response as the highest dose (7.5mg) of salbutamol but with the advantage of a lower side effects profile, high dose salbutamol causing well documented adverse events such as tremor, tachycardia and palpitations. Compared to placebo, even the lowest dose (0.4mg) of RPL554 was found to produce a significant bronchodilatory response. These results suggest that RPL554 might be a very useful new addition for the treatment, either alone or in combination, of hospitalised patients with an acute attack of asthma or COPD exacerbation.

Phase IIa in COPD

Results from RPL554 in Phase Ia COPD trial due 2Q 2016

Recruitment of 30 patients into a double-blind cross-over Phase IIa COPD study was completed in November 2015. Patients received nebulised RPL554 or placebo in addition to standard of care bronchodilators in order to identify whether RPL554 produces an additive bronchodilatory effect. The results of this trial are due to be reported in 2Q 2016.

Conclusion and next steps

Verona has made great strides over the last 18 months in the clinical development of RPL554 for respiratory disease

- The new formulation of RPL554 is safe and well tolerated even at high doses – no maximum tolerated dose was identified
- Pronounced broncholdilatory effect and improved lung function in stable COPD patients
- High dose RPL554 produced a bronchodilatory response equivalent to high dose salbutamol used to treat an outbreak of asthma or COPD in the emergency department, but with a lower level of adverse events

Great strides have been made in the de-risking of RPL554

These results provide important information towards the protocol design of the much larger pivotal Phase IIb clinical trial planned to commence early in 2017. They represent another significant step in the de-risking of RPL554.

Future development plan for RPL554 in COPD
Phase IIb trial – to start early in 2017
Confirm improved lung function and reduced symptoms
Confirm shorter hospital stays
Reduce 30 day re-admission rates

Source: Verona Pharma

Disclaimer

Hardman & Co provides professional independent research services. Whilst every reasonable effort has been made to ensure that the information in the research is correct, this cannot be guaranteed.

The research reflects the objective views of the analysts named on the front page. However, the companies or funds covered in this research may pay us a fee, commission or other remuneration in order for this research to be made available. A full list of companies or funds that have paid us for coverage within the past 12 months can be viewed at http://www.hardmanandco.com/

Hardman & Co has a personal dealing policy which debars staff and consultants from dealing in shares, bonds or other related instruments of companies which pay Hardman for any services, including research. They may be allowed to hold such securities if they were owned prior to joining Hardman or if they were held before the company appointed Hardman. In such cases sales will only be allowed in limited circumstances, generally in the two weeks following publication of figures.

Hardman & Co does not buy or sell shares, either for its own account or for other parties and neither does it undertake investment business. We may provide investment banking services to corporate clients.

Hardman & Co does not make recommendations. Accordingly, we do not publish records of our past recommendations. Where a Fair Value price is given in a research note this is the theoretical result of a study of a range of possible outcomes, and not a forecast of a likely share price. Hardman & Co may publish further notes on these securities/companies but has no scheduled commitment and may cease to follow these securities/companies without notice.

Nothing in this report should be construed as an offer, or the solicitation of an offer, to buy or sell securities by us.

This information is not tailored to your individual situation and the investment(s) covered may not be suitable for you. You should not make any investment decision without consulting a fully qualified financial adviser.

Hardman Research Ltd, trading as Hardman & Co, is an appointed representative of Capital Markets Strategy Ltd and is authorised and regulated by the Financial Conduct Authority (FCA) under registration number 600843. Hardman Research Ltd is registered at Companies House with number 8256259. However, the information in this research report is not FCA regulated because it does not constitute investment advice (as defined in the Financial Services and Markets Act 2000) and is provided for general information only.

Hardman & Co Research Limited (trading as Hardman & Co)
11/12 Tokenhouse Yard
London
EC2R 7AS
T +44 (0) 207 929 3399

Follow us on Twitter @HardmanandCo

(Disclaimer Version 2 – Effective from August 2015)

Hardman & Co

11/12 Tokenhouse Yard
London
EC2R 7AS
United Kingdom

Tel: +44(0)20 7929 3399
Fax: +44(0)20 7929 3377

www.hardmanandco.com