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TRANSFORMING THE LIVES OF AIRWAYS DISEASE PATIENTS

VR475

Top line Results

Analyst Call : Agenda

1. **Welcome and introduction:** *James Ward-Lilley*

2. **Top line results for VR475 overview:** *Gonzalo De Miquel*

3. **Q&A**: *James Ward-Lilley, Chief Executive Officer*
   Paul Fry, Chief Financial Officer
   Gonzalo De Miquel, Chief Medical Officer

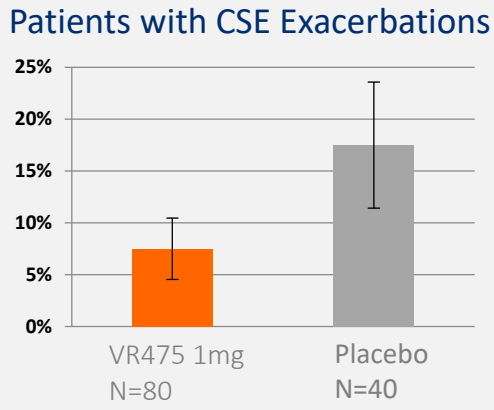
Study context

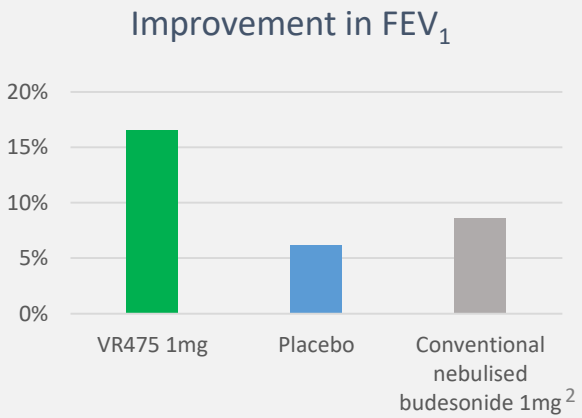
Study outline:

- **Objective**: to show a reduction in the rate of Clinically Significant Exacerbations (CSE)* of VR475 1mg vs placebo
- **Indication**: for adult and adolescent patients with severe uncontrolled asthma and a history of at least 2 exacerbations in the preceding year, despite stable treatment with high-dose ICS and at least a second controller medication
- **Positioning**: Add-on maintenance treatment before initiation of biologics or OCS

*CSE: Episode of asthma symptoms' deterioration requiring an emergency room visit and/or hospitalisation and/or systemic steroid usage

Supporting Phase II Results[1]:





1. Vogelmeier et al. 2015 - Nebulised budesonide using a novel device in patients with oral steroid-dependent asthma . Eur Respir J. 2015 May; 45(5):1273-82.
2. Patients treated with 1mg/2ml bud delivered by conventional nebuliser, PARI LC Sprint®

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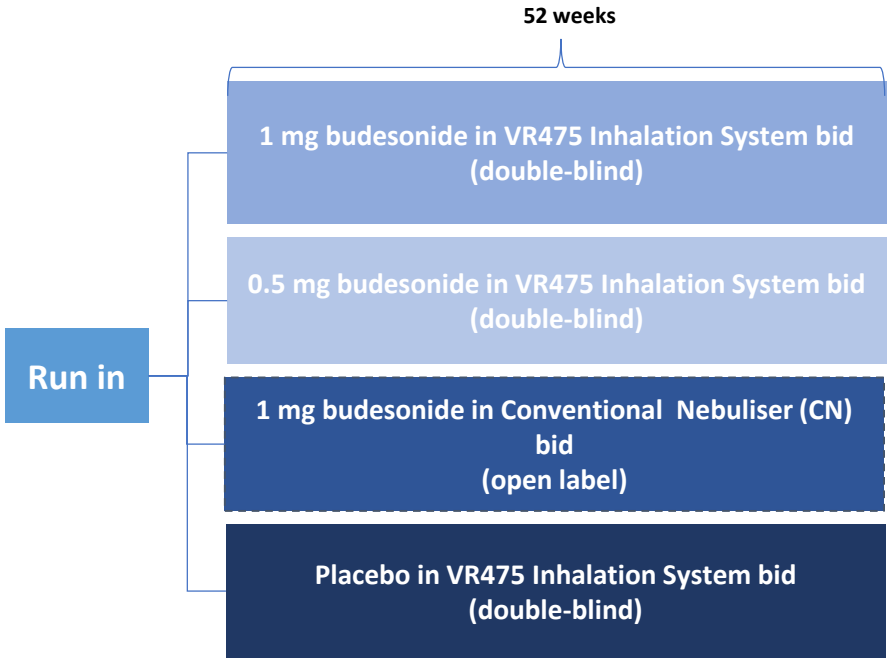
VR475 Phase III study design



Total=713 asthmatics (10% adolescents)
Randomisation= 2:1:2:1
9 countries; 105 sites

Patient population: uncontrolled asthmatics (FEV_1 <80% predicted, and symptomatic according ACQ5[1]), despite high doses of ICS and second controller
Stat assumptions: study powered 80% to show (≥40%) superiority vs. placebo on Primary Endpoint.

[1] ACQ5 – Asthma Control Questionnaire 5-item

Primary endpoint:

- Annualised rate of clinically significant exacerbations during Treatment Period vs. placebo

Key Secondary endpoints include:

- Change from baseline in pre-bronchodilator FEV_1
- ACQ-5[1]
- Rescue medication

Powering

- The study was powered to show a 40% reduction in CSE for VR475 1 mg vs placebo

VR475 Phase III top line results and next steps

- Study failed to achieve statistical significance for VR475 1mg vs placebo in the primary endpoint, but showed a positive trend
- Initial review of the available secondary endpoints and the safety data show certain endpoints achieving statistically significant and clinically meaningful differences between VR475 and placebo and versus conventionally nebulised budesonide
- Results reinforce the differential characteristics of our guided inhalation system versus conventional nebulisation
- Safety profile is consistent with known profile of budesonide
- As previously acknowledged, this was an ambitious study with a challenging endpoint
  - The indication studied in this clinical trial, where VR475 is provided as an add-on maintenance therapy to prevent exacerbations in severe uncontrolled asthma patients, is an unprecedented indication for nebulised budesonide
- Group plans to present and publish full Phase III VR475 data
- Vectura plans to terminate further development of VR475

VR475 results do not impact VR647 development programme

VR475 (EU)

A new treatment for adult and adolescent patients with budesonide, trying to show a benefit over and above its current indication and clinical utility in adult and adolescent patients with difficult-to-treat uncontrolled severe asthma

Missed Primary Endpoint. MAA plans cancelled

VR647 (US)

Nebulised steroid for paediatric asthma. Reproduce the approved efficacy profile of budesonide in a paediatric setting but with a faster administration with lower steroid burden

Positive Phase II & partnering discussions ongoing

An initial review of the available secondary endpoints and the safety data supports our confidence in the differential characteristics of our guided inhalation system. Vectura plans to progress VR647 programme as previously anticipated

Financial impact

- Based on the results Vectura will not progress further with development or partnering discussions for VR475
- There will be no impact to EBITDA in 2018 results following this decision
- As part of the acquisition of Activaero in March 2014, Vectura recognised an intangible asset for the VR475 programme. The carrying value of the intangible asset is £40m and the related deferred tax liability is £11m
- This asset will be fully impaired in the current financial year, resulting in a negative impact on the Group's loss before tax of £40m, and loss after tax of £29m
- We expect the net impact to 2019 EBITDA of revenue and R&D cost movements to be broadly neutral, as a result of our decision to cease development of VR475
- 2019 R&D guidance will be communicated as part of a trading update early in the New Year

Key messages

- In a well designed & well executed study, despite positive trend data, the primary end point of clinically significant reduction in exacerbations vs placebo was not reached
- Vectura has decided not to progress further the development or partnering of VR475
- Vectura will account for an impairment charge of £40m in 2018
- With respect to 2019, we expect the net impact to EBITDA of revenue and R&D cost movements to be broadly neutral, as a result of our decision to cease development of VR475
- Available secondary endpoints and the safety data show certain endpoints achieving statistically significant and clinically meaningful differences between VR475 and placebo and vs. conventionally nebulised budesonide
- Results reinforce the differential characteristics of our guided inhalation system versus conventional nebulisation and confidence in the ongoing VR647 programme and three additional early stage nebulisation programmes, using non budesonide molecules, announced earlier this year

News flow 2019

Pipeline:

- VR315 clinical trial results and resubmission
- VR647 partnering
- Further disclosure of new Vectura Enhanced nebulisation projects
- QVM149 PH III results and submission
- US GSK patent litigation trial outcome

Business:

- Trading update January
- Preliminary results – March
- Interim results – September

Q&A

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