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HVIVO PLC
("hVIVO" or the "Company")

hVIVO announces data from two Phase IIa clinical studies to further profile PrEP Biopharm's PrEP-001 as a potential prophylactic against the common cold

hVIVO plc (AIM: HVO), a specialty biopharma company with discovery and clinical testing capabilities, announces data from two exploratory Phase IIa studies of PrEP Biopharm's PrEP-001 as a prophylactic against the human rhinovirus 16 (HRV-16), a pathogen associated with the common cold. hVIVO holds a significant equity stake in PrEP Biopharm Limited, a UK biotech company developing drugs to treat respiratory infectious disease. PrEP-001 is a novel, nasally administered, broad-spectrum agent designed to leverage the body's innate immune system to prevent respiratory tract viral infections. Following the previously reported positive proof of concept studies in healthy volunteers challenged with influenza (2016)¹ and HRV-16 (2014), these additional Phase IIa studies were designed to further profile PrEP-001 in a specific patient population, namely people with asthma, and to explore optimal dosing schedules.

Highlights

Study PrEP-CS-002

- Double-blind, randomised, placebo controlled study, conducted in 40 patients with mild-moderate controlled asthma challenged with HRV-16
- The primary endpoint was a patient assessed Total Symptom Score (TSS)², and a statistically significant difference compared to placebo was not met in the intent to treat (ITT) population
- However, there was a statistically higher number of patients who had no symptoms (zero TSS) in the active group (5/19, 26.3%) compared to the placebo group (0/20, 0%) (Fisher Exact Test, $p=0.002$), suggesting a strong responder subgroup was present³
- In addition, analysis of a modified ITT, which excluded two significant outliers, showed that the TSS peak was significantly lower in the active compared to the placebo group ($p=0.031$)
- Further analysis of this subset of responders to fully characterise the observed results will be undertaken to determine next steps
- PrEP-001 was well tolerated – The adverse event profile was similar in active and placebo arms and was consistent with previous studies with the drug
- Further development plans for the drug to be communicated later in the year

Study PrEP-CS-003

- Double-blind, randomised, placebo-controlled study, conducted in 96 healthy subjects challenged with HRV-16, exploring the impact of two potential dosing schedules for PrEP-001 on the duration of the prophylactic effect
 - PrEP-001 was dosed either seven and six days prior to viral inoculation or four and three days before inoculation using the dose of 6400 mcg
- The primary endpoint was the difference in patient assessed TSS – There was no statistically significant difference between the two dosing schedules and placebo, suggesting once daily dosing may be a more appropriate dosing regimen
- PrEP-001 was well tolerated – The adverse event profile was similar in active and placebo arms and was consistent with previous studies with the drug

Kym Denny, CEO of hVIVO, commented;

“While PrEP-CS-002 and PrEP-CS-003 did not meet their primary endpoints, these exploratory studies provide valuable insights for PrEP-001 and build on the profile of the drug following the previously reported positive proof of concept trials in flu and the common cold. We are encouraged by signs of a potential treatment effect in the asthma responder subgroup for this complex respiratory disease where multiple phenotypes are recognised but not fully understood. PrEP Biopharm will now undertake further clinical characterisation of the results to inform the Company’s future development of PrEP-001. I look forward to updating the market on future plans later in the year.”

Further details on the study design

PrEP-CS-002: *A Phase IIa, Double-Blinded, Randomised, Controlled Study to Examine the Prophylactic Efficacy, Safety and Tolerability of PrEP-001 in Asthmatic Subjects Subsequently Challenged with Human Rhinovirus (HRV-16)*

This study was conducted in subjects with GINA⁴ 1 to 3 controlled asthma challenged with HRV-16. It was designed as a two-part study, consisting of a viral challenge arm and a safety arm. The viral challenge arm consisted of a double-blind placebo controlled study (N=19 active, N=20 placebo) with two days of dosing followed by viral challenge. Individuals were then quarantined for 8 days post-inoculation. Symptoms were self-assessed through diary cards consisting of a total of 10 upper and lower respiratory and systemic symptoms, using a 4-point scale for severity assessment. The safety arm consisted of two arms with two doses, (6400 and 12800 mcg; N=20); in the first arm 6 subjects received 6400 mcg and 4 placebo and in the second arm 6 received 12800 mcg and 4 placebo.

The primary objective of the trial was to assess the prophylactic effect of repeated intranasal dosing with PrEP-001 in subjects with asthma subsequently challenged with HRV-16 on the changes in clinical symptoms following HRV infection, when compared to placebo. The primary endpoint was the difference in the “area under the curve” of TSS, post viral challenge, between the treatment arm and the placebo arm. Secondary endpoints included symptom severity, peak and duration of symptoms, viral load/shedding (qPCR), rates of infectivity, seroconversion and lab confirmed HRV-illness, change in peak expiratory flow (PEF), nasal discharge weight and AE profile. Exploratory end points included evaluation of various blood and nasal lining fluid biomarkers, which will be reported at a future date.

PrEP-CS-003: *A Phase IIa, Randomised, Double-Blind, Placebo-Controlled Study Using Outpatient Setting to Investigate the Duration of Effect and Evaluate Further Safety of PrEP-001 Given Prophylactically in Healthy Subjects, Subsequently Challenged with Human Rhinovirus (HRV-16)*

This dose regimen and duration (i.e., durability) study was a double-blind-placebo controlled study in which there were two days of dosing with 2 different dosing regimens, followed by viral challenge (Cohort A: dosing on days -7 and -6, active n=25 and placebo n=27; Cohort B: dosing on days -4 and -3, active n=24 and placebo n=26). The study utilised an outpatient setting where individuals self-monitored symptoms from the time of first dosing until 8 days post inoculation. Symptoms were self-assessed through diary cards three times daily (4-point scale, with 10 upper and lower respiratory and systemic symptoms).

The primary objective of the study was to assess the duration of prophylactic effect of repeated intranasal dosing with PrEP-001 in healthy subjects, subsequently challenged with HRV-16, when compared to placebo, at the two different dosing regimens. The primary end-point was the difference in the “area under the curve” of TSS, post-viral challenge, between the treatment arm and placebo arm, while the secondary end points included severity, peak and duration of symptoms.

References

¹ [hVIVO confirms favourable results for PrEP Biopharm's PrEP-001 Phase IIa influenza prophylaxis study](#) (14 June 2016)

² Total Symptom Score (TSS) is the sum of the total symptom scores from day 1 to day 8, inclusive, using the 10-point symptom diary card

³ All five 'zero' TSS subjects were confirmed to be HRV-16 infected

⁴ Global Initiative for Asthma (GINA). Global strategy for asthma management and prevention – updated December 2016; <http://www.ginasthma.org/>

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Notes to Editors:

hVIVO plc (“hVIVO”), a specialty biopharma company with discovery and clinical testing capabilities, is pioneering a human-based analytical platform to accelerate drug discovery and development in respiratory and infectious diseases. Leveraging human disease models in flu, RSV and asthma exacerbation, the hVIVO platform captures disease in motion, illuminating the entire disease life cycle from healthy to sick and back to health. Based in the UK, market leader hVIVO has conducted more than 45 clinical studies, inoculated over 2000 volunteers and has three first-in-class therapies currently in development with a growing pre-clinical pipeline.