Publication of Positive Results in Journal

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Open Orphan plc

("Open Orphan" or the "Company")

Positive results from Phase IIb field study of FLU-v vaccine (FLU-v 003), which has been developed by Imutex Limited, hVIVO's 49% joint venture with the SEEK Group. FLU-v is a first-in-class 'universal', broad spectrum, standalone, influenza vaccine candidate and the results have now been published in a peer review journal

- *The publication in the Annals of Internal Medicine journal concluded adjuvanted FLU-v is immunogenic and merits Phase III development to explore efficacy*
- *Compelling data package from two Phase II studies shows that a single dose of adjuvanted FLU-v induces cellular and antibody responses (FLU-v 003) and that it has a clinical impact in reducing disease, symptom and viral load (FLU-v 004)*
- *Imutex currently scheduling meetings with key regulatory authorities, FDA and EMEA, hoping to gain confirmation of the remaining development pathway to approval for FLU-v*

10 March 2020: Open Orphan plc (ORPH) the rapidly growing specialist CRO pharmaceutical services company which has a focus on orphan drugs and is a world leader in the provision of virology and vaccine challenge study services, today announces publication of positive results of a Phase IIb field study of FLU-v 003 (Study 003, NCT02962908) in the *Annals of Internal Medicine* journal. The headline results from this study were previously announced by hVIVO on 18 June 2018. FLU-v is being developed by Imutex Limited, hVIVO's 49% joint venture with the SEEK Group.

The Primary and secondary endpoints were achieved in a Phase IIb study, done within the UNISEC* Consortium and funded by the European Commission under the Seventh Framework Programme for Research and Technological Development (FP7). 175 healthy adults were randomly assigned to either an injection of adjuvanted (1 dose) or nonadjuvanted (2 doses) FLU-v or adjuvanted or nonadjuvanted placebo to compare the safety, immune response, and exploratory efficacy of different formulations and dosing regimens. They found that a single dose of adjuvanted FLU-v elicited a greater immune response compared with placebo. Adverse events were mostly mild to moderate injection site reactions. The authors conclude that a Phase III trial is warranted to explore efficacy.

*Universal Influenza Vaccines Secured, European Union funded consortium for the advancement of universal influenza vaccines.

Trevor Phillips, CEO of Open Orphan, said:

"FLU-v is a universal influenza vaccine that targets conserved internal regions of the flu virus. There have been two positive Phase II studies; FLU-v 003, testing immunogenicity and FLU-v004, testing efficacy in a human challenge study. Both Phase II studies, FLU-v 003 and FLU-v 004 are externally supported by UNISEC and NIAID (National Institute of Allergy and Infectious Diseases, part of the U.S. National Institutes of Health) respectively which gives strong external endorsement from key EU and US organisations. The full results from this positive Phase II immunogenicity study underscores both our, and our partner SEEK's, confidence in the potential of FLU-v as a universal flu vaccine.

The advantages of FLU-v over the seasonal flu vaccine are that the composition of the FLU-v vaccine will remain the same year after year and it is manufactured synthetically, enabling year-round manufacturing and thus, increasing the number of doses available worldwide. It will not be subject to a strict vaccination window as is the case with seasonal flu vaccines. Also, being a universal vaccine, it should provide protection against new strains of flu virus which the seasonal flu vaccine is not able to do.

Imutex continues to explore options for the FLU-v vaccine programme and is scheduling meetings with key regulatory authorities, FDA and EMEA, hoping to gain further insight into Phase III preparation, a key area of interest expressed by potential partners."

Cathal Friel, Executive Chairman of Open Orphan, said:

"The market potential for a broad spectrum universal influenza vaccine is significant and has become increasingly important and valuable in recent weeks when governments around the world are finally waking up and realising that universal flu vaccines need to be commercialised and there must be a better way forward than reliance on the traditional annual flu vaccination process which has variable efficacy, offers little protection against emerging strains and is available in limited quantities. A universal flu vaccine can and should be targeted at the entire population base. We now await publication of the positive results data from the NIAID FLU-v study (004) in a peer reviewed journal while still focusing on the Company's strategy of achieving profitability in the near term and as we target the rapidly growing CRO pharmaceutical services sector.

As previously announced to the market, the newly enlarged Open Orphan group, of which hVIVO is a subsidiary of, is now very much targeted upon delivering a profitable pharmaceutical services business and will no longer be spending shareholders' funds on the drug discovery processes. The additional investment or cost associated with commercialising FLU-v, will come from out-licencing the final stages including Phase III trials of FLU-v's study, to major international pharmaceutical companies, in Europe, North America, and very importantly also in China. But we are increasingly excited about FLU-v potentially finally entering phase III clinical trials and now is one of the most opportune times to be doing that."

Abstract: http://annals.org/aim/article/doi/10.7326/M19-0735

Immunogenicity, Safety, and Efficacy of a Standalone Universal Influenza Vaccine, FLU-v, in Healthy Adults
A Randomized Clinical Trial

Background: FLU-v is a broad-spectrum influenza vaccine that induces antibodies and cell-mediated immunity.

Objective: To compare the safety, immunogenicity, and exploratory efficacy of different formulations and dosing regimens of FLU-v versus placebo.

Design: Randomized, double-blind, placebo-controlled, single center phase 2b clinical trial. ClinicalTrials.gov: NCT02962908; EudraCT: 2015-001932-38

Setting: The Netherlands.

Participants: 175 healthy adults aged 18 to 60 years.

Intervention: 0.5-mL subcutaneous injection of 500 µg of adjuvanted (1 dose) or nonadjuvanted (2 doses) FLU-v (A-FLU-v or NA-FLU-v) or adjuvanted or nonadjuvanted placebo (A-placebo or NA-placebo) (2:2:1:1 ratio).

Measurements: Vaccine-specific cellular responses at days 0, 42, and 180 were assessed via flow cytometry and enzyme linked immunosorbent assay. Solicited information on adverse events (AEs) was collected for 21 days after vaccination. Unsolicited information on AEs was collected throughout the study.

Results: The AEs with the highest incidence were mild to moderate injection site reactions. The difference between A-FLU-v and A-placebo in the median fold increase in secreted interferon--γ (IFN-γ) was 38.2-fold (95% CI, 4.7- to 69.7-fold; P = 0.001) at day 42 and 25.0-fold (CI, 5.7- to 50.9-fold; P < 0.001) at day 180. The differences between A-FLU-v and A-placebo in median fold increase at day 42 were 4.5-fold (CI, 2.3- to 9.8-fold; P <0.001) for IFN-γ -producing CD4+ T cells, 4.9-fold (CI, 1.3- to 40.0-fold; P < 0.001) for tumour necrosis factor-α (TNF-α), 7.0-fold (CI, 3.5- to 18.0-fold; P < 0.001) for interleukin-2 (IL-2), and 1.7-fold (CI, 0.1- to 4.0-fold; P = 0.004) for CD107a. At day 180, differences were 2.1-fold (CI, 0.0- to 6.0-fold; P = 0.030) for IFN-γ and 5.7-fold (CI, 2.0- to 15.0-fold; P < 0.001) for IL-2, with no difference for TNF-α or CD107a. No differences were seen between NA-FLU-v and NA-placebo.

Limitation: The study was not powered to evaluate vaccine efficacy against influenza infection.

Conclusion: Adjuvanted FLU-v is immunogenic and merits phase 3 development to explore efficacy.

Primary Funding Source: SEEK and the European Commission Directorate-General for Research and Innovation, European Member States within the UNISEC (Universal Influenza Vaccines Secured) project.

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Notes to Editors:

Open Orphan is a rapidly growing specialist CRO pharmaceutical services company which has a focus on orphan drugs and is a world leader in the provision of virology and vaccine challenge study services and viral laboratory services. It has Europe's only 24-bedroom quarantine clinic with onsite virology lab in Queen Mary's Hospital London. hVIVO supports product development for customers developing antivirals, vaccines and respiratory therapeutics, all particularly relevant and topical in the environment of heightened awareness of the Coronavirus in 2020. The Company also has a leading portfolio of 8 viral challenge study models which are: 2 FLU, 2 RSV, 1 HRV, 1 Asthma, 1 cough and 1 COPD viral challenge models. No other company in the world has such a portfolio, with only two competitors globally having 1 challenge study model each.

Open Orphan comprises of two commercial specialist CRO services businesses (Venn and hVIVO) and is developing an early stage orphan drug genomics data platform business. This platform captures valuable genetic data from patient populations with specific diseases with designated orphan drug status and incorporating AI tools. In June 2019, Open Orphan acquired AIM-listed Venn Life Sciences Holdings plc in a reverse take-over and in January 2020 it completed the merger with hVIVO plc. Venn, as an integrated drug development consultancy, offers CMC (chemistry, manufacturing and controls), preclinical, Phase I & II clinical trials design and execution. The merger with hVIVO created a European full pharma services company broadening the Company's customer base and with complementary specialist CRO services, widened the range of the Company's service offerings.

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