PRESS RELEASE

For media and investors only

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GSK starts Phase III RSV candidate vaccine programme for older adults

- RSV-associated lower respiratory tract-diseases (LRTDs) are estimated to cause around 360,000 hospitalisations and 24,000 deaths in older adults (60+) annually in developed countries
- First Phase III study evaluates the immunogenicity, safety, reactogenicity and persistence, to be followed by a separate Phase III study assessing vaccine efficacy
- Positive Phase I/II results established the robust immunogenicity of the vaccine candidate in the target population

GlaxoSmithKline plc (LSE/NYSE: GSK) today announced that patient dosing has begun in a Phase III clinical programme investigating the immunogenicity, safety, reactogenicity and persistence of its Respiratory Syncytial Virus (RSV) candidate vaccine for older adults (GSK3844766A), following the release of positive Phase I/II results on safety, reactogenicity and immunogenicity (presented at ID Week Congress in October 2020).

RSV represents a significant health threat for older adults (>60 years of age), with 360,000 hospitalisations and 24,000 deaths associated with RSV infections estimated annually in developed countries[1]. Without routine testing for RSV and robust surveillance systems in several countries, global data on the burden of RSV in older adults is either lacking or is likely to largely underestimate its significance. As the global population ages, the morbidity and mortality of respiratory infections including RSV are expected to steadily increase. An RSV vaccine for older adults would help prevent primary infection and also help preserve independence, health and quality of life.

Emmanuel Hanon, Senior Vice President and Head of Vaccines R&D for GSK, said: “RSV is one of the most significant remaining unmet medical needs for older adults, with 1 out of 6 infected with RSV requiring a hospitalisation[2]. With our unique combination of technologies, the pre-fusion F antigen and our proprietary adjuvant system, we were able to induce a strong immune response, of both humoral and cellular components, to levels normally seen in healthy adults”.

The RSV candidate vaccine for older adults contains a recombinant subunit pre-fusion RSV antigen (RSVPreF3) combined with GSK’s proprietary AS01 adjuvant[3], which is also used in GSK’s shingles vaccine. The candidate vaccine has shown promising safety and immunogenicity in a Phase I/II study in both young and older adults and was well-tolerated (data presented at the ID Week Congress in October 2020). The results showed that one month post-immunisation, the candidate vaccine had elicited a robust humoral and cellular immunity compared with baseline, with a close to 10 times increase of RSV-A neutralising antibodies and above 12 times increase of RSVPreF3 IgG antibodies induced in the vaccinated group. These results show that the vaccine candidate can stimulate the immune system in older adults to produce a similar level of antibodies as young adults, which is crucial to protect this vulnerable population. In addition, the candidate vaccine was able to restore the

[1] Shi T. et al, *Journal of Infectious Diseases*, 2020, October 2; 222 (supplement 7): S577-S583; Data presented at the 7th ESWI Influenza Conference, 6–9 December 2020

[2] Shi T. et al, *Journal of Infectious Diseases*, 2020, October 2; 222 (supplement 7): S577-S583

[3] The GSK proprietary AS01 adjuvant system contains QS-21 Stimulon™ adjuvant licensed from Agenus Inc. (NASDAQ: AGEN)

lower levels of pre-existing RSV-specific T-cells observed in older adults before vaccination to similar levels observed in the younger adults following vaccination.

This candidate vaccine is part of a portfolio of RSV vaccines in development by GSK, which includes maternal and paediatric vaccine candidates. To deliver a broad benefit against RSV infections, the three candidate vaccines are based on different novel technologies, tailored to the needs of the different populations most impacted. All three candidate vaccines have received FDA fast-track designation. The Phase III efficacy study for the maternal RSV candidate vaccine started in November 2020, while the Phase I/II study (in RSV sero-naive infants) with the paediatric RSV candidate vaccine is ongoing.

About the AReSVi Study

The study named AReSVi 004 is a randomised open-label Phase III study (NCT04732871) to be conducted in up to 1650 adults and will assess the safety, reactogenicity, immunogenicity and long-term persistence of immune response up to 3 years following vaccination of our RSV candidate vaccine, in adults aged 60 years and above. The study is expected to end in early 2024, with interim results expected to be available in the second half of 2022.

A second study (AReSVi 006) investigating the efficacy of the candidate vaccine to help protect older adults against lower-respiratory tract disease due to RSV is expected to start in the coming months. In total, it is expected that more than 10,000 participants will be enrolled in the Phase III programme for the RSV candidate vaccine for older adults, as it is standard for late stage clinical trials where correlate of protection has not been established yet.

About GSK's RSV candidate vaccine for older adults (GSK3844766A)

This candidate vaccine contains a recombinant subunit pre-fusion RSV antigen (RSVPreF3) combined with GSK's proprietary AS01 adjuvant, which is also used in GSK's shingles vaccine. Phase I/II interim safety, reactogenicity and immunogenicity data of GSK's RSV candidate vaccine in young adults and in older adults aged 60 to 80 (NCT03814590) presented at ID Week in October 2020, showed that within one-month post-immunisation, the adjuvanted candidate vaccine as well as other vaccine formulations tested were well tolerated and induced a robust humoral and cellular immunity compared with baseline. The selected formulation of the candidate vaccine showed in the 60-80-year-old vaccines, that one-month post vaccination:

- High levels of RSVPreF3 IgG antibodies (geometric mean antibody concentrations were 12.4 fold-higher) and RSV-A neutralising antibodies (geometric mean antibody titers were 9.5 fold-higher) were induced.
- Before vaccination, deficiency of RSVPreF3-specific T-cells (hypothesised to help promote viral clearance) was observed in older adults compared to younger adults. After vaccination, a robust RSVPreF3 CD4+ T-cells response in older adults had been boosted to reach a similar range than the one observed in younger adults.

About respiratory syncytial virus

Although RSV infection can occur at any age, it can cause more serious respiratory illness in our infants and older adults. Globally, although data quality varies across different countries, there are an estimated 33 million cases of RSV annually in children less than 5 years of age, with about 3 million hospitalised and approximately 120,000 dying each year from complications associated with the infection. Nearly half of these paediatric hospitalisations and deaths occur in infants less than 6 months of age[4]. According to the Centers for Disease Control and Prevention, virtually all children in the US get an RSV infection by the time they are 2 years old and one to two out of every 100 children younger than 6 months of age with RSV infection may need to be hospitalised[5]. It also represents a significant health threat for older adults (>60 years of age), with 360,000 hospitalisations and 24,000 deaths associated with RSV infections estimated annually in developed countries[6]. Every year,

[4] Shi T. et al, *Lancet*. 2017;390:946–58
[5] CDC - https://www.cdc.gov/rsv/high-risk/infants-young-children.html
[6] Shi T. et al, *Journal of Infectious Diseases*, 2020, October 2; 222 (supplement 7): S577-S583; Data presented at the 7th ESWI Influenza Conference, 6–9 December 2020

approximatively 1 million people globally over 65 die from respiratory infections[7] and about 1 in 6 older adults infected with RSV will require hospitalisation[8].

Without robust surveillance systems in several countries, global data on the burden of RSV in older adults is either lacking or likely to underestimate its significance. As the global population ages, the morbidity and mortality of respiratory infections including those related to RSV are expected to steadily increase.

About GSK

GSK is a science-led global healthcare company with a special purpose: to help people do more, feel better, live longer. For further information please visit www.gsk.com/about-us.

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[7] GBD 2015 LRI Collaborators. Estimates of the global, regional, and national morbidity, mortality, and aetiologies of lower respiratory tract infections in 195 countries: a systematic analysis for the Global Burden of Disease Study 2015. Lancet Infect Dis 2017; 17(11):1133-1161.
[8] Shi T. et al, *Journal of Infectious Diseases*, 2020, October 2; 222 (supplement 7): S577-S583