



# GSK announces US regulatory submission of candidate vaccine for prevention of shingles

24 October 2016

## Regulatory submissions in the EU and Canada remain on track for 2016

GlaxoSmithKline plc (LSE/NYSE: GSK) today announced that it has submitted a Biologics License Application (BLA) for its candidate shingles vaccine, Shingrix™, to the United States Food and Drug Administration (FDA), seeking approval for the prevention of herpes zoster (shingles) in people aged 50 years or over.

The candidate vaccine is a non-live, recombinant vaccine to help prevent shingles and its complications. The phase III clinical trial programme showed that by reducing the incidence of shingles, the candidate vaccine also reduced the overall incidence of postherpetic neuralgia (PHN), a form of chronic pain associated with shingles. Regulatory approval is being sought for the vaccine to be given intramuscularly in two doses, with a two to six month interval between doses.

Dr Emmanuel Hanon, Senior Vice President and Head of Vaccines R&D, GSK said: “Shingles is a common and potentially serious condition. It can cause lasting pain and other complications such as scarring or visual impairment, which can severely impact the quality of people’s lives. The risk of developing shingles increases with age and it is estimated that up to one in every three people is at risk. Today’s file submission puts us a step closer to making this vaccine available to help protect more people from shingles and the complications associated with it.”

The regulatory submission for Shingrix is based on a comprehensive phase III clinical trial programme evaluating its efficacy, safety and immunogenicity in more than 37,000 people. This includes the ZOE-50 and ZOE-70 studies published in the New England Journal of Medicine in April 2015 and September 2016, respectively.<sup>1,2</sup>

The candidate vaccine is one of the more than 40 assets profiled to investors at GSK’s R&D event in November 2015 and belongs to the company’s vaccines portfolio – one of six core

areas of scientific research and development alongside oncology, immuno-inflammation, and infectious, respiratory and rare diseases.

Regulatory submissions in the European Union and Canada are on track for 2016 and planned for Japan in 2017. GSK's shingles candidate vaccine is not currently approved for use anywhere in the world.

## About the phase III study programme

Involving more than 37,000 subjects globally, the phase III programme evaluated the efficacy, safety and immunogenicity of two doses of GSK's candidate shingles vaccine given intramuscularly two months apart in older adults. Data from all the completed studies has been included in the regulatory file:

The ZOE-50 (ZOster Efficacy in adults aged 50 years and over) (NCT01165177) trial of 16,160 adults aged 50 years and older studied overall vaccine efficacy against shingles compared to placebo. The data were published in April 2015 in the NEJM.<sup>1</sup>

The ZOE-70 (ZOster Efficacy in adults aged 70 years and over) (NCT01165229) trial of more than 14,800 adults aged 70 years and older studied overall vaccine efficacy against shingles compared to placebo. Additionally, a pooled analysis of data from the ZOE-70 and ZOE-50 trials assessed overall vaccine efficacy in reducing the risk of developing shingles and PHN in people aged 70 years and over. These data were published in September 2016 in the NEJM.<sup>2</sup>

A clinical study is also underway to evaluate revaccination in subjects who have previously been vaccinated against shingles with the currently available live-attenuated vaccine. Additional trials are underway in solid and haematological cancer patients, haematopoietic stem cell and renal transplant recipients and HIV-infected people. These studies will provide additional information on the candidate vaccine's safety and ability to stimulate immune responses in populations at high risk of shingles because of the weakening of their immune system.

## About Shingrix

The candidate vaccine is a non-live, recombinant vaccine to help prevent herpes zoster and its complications and combines glycoprotein E, a protein found on the varicella zoster virus (VZV) that causes shingles, with an adjuvant system, AS01<sub>B</sub>, which is intended to enhance the immunological response to the antigen<sup>3</sup>. GSK intends to register the product as Shingrix<sup>TM</sup>, subject to approval by relevant regulatory review bodies. The name Shingrix has been approved by the European Medicines Agency.

## About shingles

Shingles typically presents as a painful, itchy rash that develops on one side of the body, as a result of reactivation of latent chickenpox virus (varicella zoster virus or VZV). Data from many countries indicates that more than 90% of adults have been infected with varicella during childhood. The individual lifetime risk of developing shingles is approximately one in three for people in the USA; however, this increases to one in two people aged 85 and over. A person's risk for shingles increases sharply after 50 years of age due to a natural age-related decline in immune system function, or as a consequence of an underlying immunocompromising condition.<sup>4</sup>

The most common complication from shingles is post-herpetic neuralgia, defined as a localised pain of significant intensity persisting at least 90 days after the appearance of the acute shingles rash. Other complications of shingles include ophthalmologic, neurological and cutaneous disease, which can result in severe disability.<sup>5</sup>

## References

1. Lal et al., N Engl J Med 2015; 372:2087-2096 Efficacy of an Adjuvanted Herpes Zoster Subunit Vaccine in Older Adults.
2. Cunningham et al., N Engl J Med 2016; 375: 1019-32. Efficacy of the herpes zoster subunit vaccine in adults 70 years of age or older.
3. The GSK proprietary AS01 adjuvant system contains QS-21 Stimulon® adjuvant licensed from Antigenics LLC, a wholly owned subsidiary of Agenus Inc. (NASDAQ: AGEN), MPL and liposomes.
4. Shingles (Herpes Zoster) Clinical Overview. US Centers for Disease Control and Prevention. Accessed at: <http://www.cdc.gov/shingles/hcp/clinical-overview.html> on 6 Sept 2016.
5. Cohen et al., N Engl J Med 2013;369:255-63 Clinical practice: Herpes zoster.

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## Cautionary statement regarding forward-looking statements

GSK cautions investors that any forward-looking statements or projections made by GSK, including those made in this announcement, are subject to risks and uncertainties that may cause actual results to differ materially from those projected. Such factors include, but are not limited to, those described under Item 3.D 'Risk factors' in the company's Annual Report on Form 20-F for 2015.

## Contact info