

## **Novartis candidate vaccine Bexsero<sup>®</sup> shows significant potential in providing broad coverage against meningococcal serogroup B infections**

- *Pivotal study in more than 1,800 infants shows Bexsero induces robust immune response when given alone or with other routine vaccines in different vaccination schedules<sup>1</sup>*
- *Meningococcal serogroup B disease has highest incidence in infants and young children<sup>2</sup> and can lead to death within 24-48 hours of first symptoms<sup>3</sup>*
- *Bexsero can help protect the majority of people at risk for infection, as data show the vaccine also induces robust immune response in toddlers and adolescents<sup>1, 4, 5, 6, 7</sup>*

**Basel, June 9, 2011** – New data from a pivotal study in more than 1,800 infants show that Novartis candidate vaccine Bexsero<sup>®</sup> (Multicomponent Meningococcal Serogroup B Vaccine) induces a robust immune response to meningococcal serogroup B when given alone or when co-administered with other routine vaccines<sup>1</sup>. These results also show that Bexsero can fit into various vaccination schedules in the first year of life<sup>1, 4</sup>, when the likelihood of contracting this often-deadly disease is greatest<sup>2</sup>. The study also demonstrated that Bexsero has an acceptable tolerability profile<sup>4</sup>.

Data from another pivotal study in more than 1,500 toddlers shows that Bexsero provides protective immune response when used as a booster in toddlers already primed, or after two doses in those not previously vaccinated with Bexsero<sup>5, 6</sup>. A third study presented showed that Bexsero induces a strong immune response in adolescents against meningococcal serogroup B (MenB)<sup>7</sup>. The data were presented at The European Society for Paediatric Infectious Diseases (ESPID) in The Hague, The Netherlands.

These data are included in the comprehensive clinical program with Bexsero in more than 8,000 infants, toddlers, adolescents and adults which served as the basis of the registration file submitted to the European Medicines Agency (EMA) in December 2010<sup>1, 4, 5, 6, 7, 8</sup>.

“MenB disease poses a significant burden to people around the world<sup>9, 10</sup>, particularly infants, the population at greatest risk for the disease<sup>2</sup>,” said Andrin Oswald, Head of Novartis Vaccines and Diagnostics Division. “The data show that Bexsero, our innovative multicomponent MenB vaccine, holds great promise in providing a solution to a major public health concern that can have a devastating impact on vulnerable populations<sup>1, 2, 4, 5, 6, 7</sup>.”

MenB is the most common cause of bacterial meningitis<sup>9, 10</sup> for which there is no effective routine vaccine<sup>2</sup>, and it is responsible for up to 90% of meningococcal disease cases in Europe<sup>11</sup>, and over 80% of meningococcal cases in infants in Canada<sup>12</sup>. Survivors may suffer permanent brain damage, learning disabilities, hearing loss, and limb loss<sup>13</sup>.

“The serious and long-term effects of MenB are often devastating to its victim, family members and the community at large<sup>13</sup>,” said Jamie Findlow PhD, Deputy Head of the Health Protection Agency, Vaccine Evaluation Unit, Manchester, UK. “The rapid disease progression<sup>3</sup> and flu-like symptoms<sup>14</sup> of MenB can be difficult to recognize, particularly in infants<sup>14</sup>, making prevention through vaccination the most effective way to control this disease<sup>9</sup>.”

Bexsero has the potential to provide protection against a broad range of MenB strains<sup>15</sup>. If licensed, Bexsero could fill a public health need across multiple regions that is not met by currently available vaccines<sup>2</sup>. Recent data have shown that Bexsero could be expected to provide protection against approximately 80% of more than 1,000 disease-causing MenB strains isolated in Europe in 2007-2008<sup>16</sup>.

### **Infant Study Design and Results**

*Novartis Study P12, ESPID Abstracts 1205 and 1187*

- This Phase IIb open-label immunogenicity study analysis randomized more than 1,800 infants to receive Bexsero at 2, 4, 6 months or at 2, 3, 4 months with or without routine vaccines (7-valent pneumococcal glyco-conjugate-vaccine and a combined diphtheria-toxoid, tetanus-toxoid, inactivated-polio, acellular-pertussis, hepatitis B and Haemophilus influenza type-b vaccine). Immune response was measured using the human serum bactericidal antibody (hSBA) assay<sup>1</sup>.
- The study met its primary endpoints, and showed that the majority of infants vaccinated with Bexsero, at either dosing schedule with or without routine vaccines, achieved hSBA  $\geq 1:5$  against all vaccine antigens in tested MenB strains (H44/76, 5/99, NZ98/254)<sup>1</sup>.
- More than 99% of participants receiving Bexsero at 2, 4, 6 months (concomitantly or without routine-vaccines) or at 2, 3 and 4 months (with routine-vaccines) developed hSBA titers  $\geq 1:5$  against strains 44/76 and 5/99. For NZ98/254 the correlate was reached or exceeded in 79% (2, 4, 6 months with routine-vaccines), 87% (2, 4, 6 months without routine-vaccines) and 81% (2, 3, 4 months with routine vaccines)<sup>1</sup>.
- Data also show that responses to the routine vaccine antigens, when co-administered with Bexsero, were generally similar, except for a slightly lower immune response to pneumococcal serotype 6B, which was not clinically meaningful<sup>1</sup>.
- The data also show that Bexsero, when administered alone, had a reactogenicity profile that was comparable to those of the routine vaccines. Fever, which is a common event following routine childhood immunizations, was observed more frequently in infants who received Bexsero together with routine infant vaccines compared to infants receiving routine vaccines alone<sup>4</sup>. Fever was generally low-grade, mild and of short duration, with more than 95% of cases resolving within 24-48 hours<sup>4</sup>.

### **Toddler Study Results and Design**

*Novartis Study P13E1, ESPID Abstracts 877 and 900*

#### *Booster*

- This Phase III, open-label immunogenicity and tolerability extension analysis included more than 1,500 toddlers who had been administered a three-dose primary series of Bexsero at 2, 4, 6 months. Toddlers were randomized to receive either a fourth (booster) dose of Bexsero concomitantly with measles, mumps, rubella, and varicella vaccine (MMR-V), or Bexsero at 12 months followed by

MMR-V at 13 months. Immunogenicity was measured using the hSBA assay and was assessed one month post booster dose<sup>5</sup>.

- This study met all primary endpoints. The data show Bexsero to be highly immunogenic in this age group against all vaccine antigens in all MenB strains tested (H44/76, 5/99, NZ98/254), with 11-19 fold increases in hSBA titers<sup>5</sup>.
- The percentage of toddlers with an hSBA  $\geq$  1:5 who received Bexsero alone or Bexsero concomitantly with MMR-V was 100% against H44/76 and 5/99, and 97% and 94% against strain NZ98/254, respectively<sup>5</sup>.
- Results show that immune responses to Bexsero and MMR-V were not affected when both vaccines were administered concomitantly, and that adverse events, notably fever, were not increased by the concomitant use of Bexsero and MMR-V<sup>5</sup>.

#### *Catch Up*

- The study also evaluated a two-dose schedule in toddlers, suitable for a catch-up vaccination, when administered alone or concomitantly with MMRV vaccine<sup>6</sup>.
- In this open-label study, healthy toddlers not previously vaccinated with Bexsero either received MMR-V at 12 months followed by two doses of Bexsero at 13 and 15 months (alone), or MMR-V and Bexsero at 12 months and Bexsero at 14 months (concomitant). Immunogenicity against three reference strains was assessed in subsets one month later by hSBA assay using human complement. Solicited post-vaccination reactions were recorded for seven days<sup>6</sup>.
- Immune responses were similar in both groups; hSBA GMTs for alone and concomitant groups were 271 and 248 against strain H44/76; 599 and 627 against strain 5/99; 43 and 32 against NZ98/254, respectively. Seroprotection rates (% hSBA  $\geq$  5) against strains H44/76, 5/99, and NZ98/254 were 100%, 100% and 96% in the concomitant group, respectively, and 100% against all three strains in the alone group<sup>6</sup>.
- Two doses of Bexsero two months apart were sufficient to elicit protective immune responses against all three reference strains for the component antigens, unaffected by concomitant MMR-V administration, with minimal impact on reactogenicity, so facilitating catch-up vaccination in current toddler vaccination schedules<sup>6</sup>.

#### **Adolescent Study Design and Results**

##### *Novartis Study P10, ESPID Abstract 905*

- In an observer-blind study, 11–17 year-old adolescents were randomized to receive one to three doses of Bexsero or placebo at baseline, one and/or two months later. Primary immunogenicity outcome was a titer  $\geq$ 4 in a serum bactericidal assay using human complement (hSBA) against three test strains selected to evaluate the contribution of individual vaccine antigens. Tolerability was assessed by solicited local and systemic reactions within seven days of each study vaccination. Adverse events were monitored throughout the study<sup>7</sup>.
- This study met all primary endpoints. One month after vaccination 92–97% of recipients of one Bexsero dose, 99–100% after two or three Bexsero doses and 29–50% of placebo recipients had hSBA titers  $\geq$ 4 against the three test strains<sup>7</sup>. Similar proportions of placebo and Bexsero recipients reported solicited local (89–94%) and systemic (70–79%) reactions after the first study injection<sup>7</sup>. Bexsero induced robust immune response and had an acceptable tolerability profile

following one, two, or three doses and in all schedules administered. No evidence of increased reactogenicity was observed with two or three doses compared with one dose of Bexsero. Fever observed in adolescents vaccinated with Bexsero was comparable to those who received placebo alone<sup>7</sup>.

### **About Meningococcal Disease**

Meningococcal disease is a sudden<sup>17</sup>, aggressive illness that can lead to death within 24-48 hours of the first symptoms<sup>3</sup>. Survivors may suffer permanent brain damage, learning disabilities, hearing loss, and limb loss<sup>13</sup>. The disease is a leading cause of bacterial meningitis<sup>9, 13</sup> – an infection of the membrane around the brain and spinal cord<sup>3</sup> – and sepsis – a bloodstream infection<sup>13</sup>. Five main serogroups of meningococcal bacteria (A, B, C, W-135 and Y) cause the majority of all cases around the world<sup>18</sup>.

Licensed vaccines are available to protect against meningococcal disease caused by serogroups A, C, W135 and Y<sup>3</sup>; however, MenB remains an important unmet public health challenge<sup>2</sup>. MenB is the most common cause of bacterial meningitis<sup>9, 10</sup> for which there is no effective routine vaccine<sup>2</sup>, and it is responsible for up to 90% of meningococcal disease cases in Europe<sup>11</sup>.

### **About Bexsero**

The Novartis Bexsero vaccine was developed using a pioneering approach known as “reverse vaccinology<sup>19</sup>.” In contrast to conventional methods of developing vaccines, reverse vaccinology decodes the genetic makeup (genome sequence) of MenB and selects those proteins that are most likely to be broadly-effective vaccine candidates<sup>19</sup>. Bexsero (also known as 4CMenB) contains multiple components, which independently are highly immunogenic and, taken together, have the potential to protect against a broad range of disease-causing strains<sup>15</sup>. To date, more than 8,000 infants, toddlers, and adults have been enrolled in studies of Bexsero<sup>1, 4, 5, 6, 7, 8</sup>.

### **Disclaimer**

The foregoing release contains forward-looking statements that can be identified by terminology such as “potential,” “can,” “promise,” “may,” “could,” or similar expressions, or by express or implied discussions regarding potential marketing approvals for Bexsero, or the timing of any such approvals, or regarding potential future revenues from Bexsero. You should not place undue reliance on these statements. Such forward-looking statements reflect the current views of management regarding future events, and involve known and unknown risks, uncertainties and other factors that may cause actual results with Bexsero to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no guarantee that Bexsero will be approved for sale in any market or at any particular time. Nor can there be any guarantee that Bexsero will achieve any particular levels of revenue in the future. In particular, management’s expectations regarding Bexsero could be affected by, among other things, unexpected regulatory actions or delays or government regulation generally; unexpected clinical trial results, including unexpected new clinical data and unexpected additional analysis of existing clinical data; competition in general; government, industry and general public pricing pressures; the company’s ability to obtain or maintain patent or other proprietary intellectual property protection; the impact that the foregoing factors could have on the values attributed to the Novartis Group’s assets and liabilities as recorded in the Group’s consolidated balance sheet, and other risks and factors referred to in Novartis AG’s current Form 20-F on file with the US Securities and Exchange Commission. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those anticipated, believed, estimated or expected. Novartis is providing the information in this press release as of this date and does not undertake any obligation to update any forward-looking statements contained in this press release as a result of new information, future events or otherwise.

### **About Novartis**

Novartis Vaccines and Diagnostics is a division of Novartis, focused on the development of preventive treatments. The division has two businesses: Novartis Vaccines and Novartis Diagnostics. Novartis Vaccines is the world's fifth-largest vaccines manufacturer and second-largest supplier of flu vaccines in the US. The division's products also include meningococcal, pediatric and travel vaccines. Novartis Diagnostics, the blood testing business, is dedicated to preventing the spread of infectious diseases through the development of novel blood-screening tools that protect the world's blood supply.

Novartis provides healthcare solutions that address the evolving needs of patients and societies. Focused solely on healthcare, Novartis offers a diversified portfolio to best meet these needs: innovative medicines, eye care, cost-saving generic pharmaceuticals, consumer health products, preventive vaccines and diagnostic tools. Novartis is the only company with leading positions in these areas. In 2010, the Group's continuing operations achieved net sales of USD 50.6 billion, while approximately USD 9.1 billion (USD 8.1 billion excluding impairment and amortization charges) was invested in R&D throughout the Group. Headquartered in Basel, Switzerland, Novartis Group companies employ approximately 119,000 full-time-equivalent associates and operate in more than 140 countries around the world. For more information, please visit <http://www.novartis.com>.

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