



# Advances in Vaccine Development for Meningococcal Serogroup B Disease

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Meningitis Research Foundation  
November 7-8, 2007  
London, UK



# Key Points

- *N. meningitidis* serogroup B has high incidence and causes meningitis outbreaks in many regions of the world
- Reverse vaccinology is an innovative approach to identifying novel antigens as vaccine candidates against meningococcal serogroup B (MenB)
- The Novartis MenB vaccine is the first based on recombinant proteins to induce a robust bactericidal immune response against a broad panel of disease-causing strains
- The Novartis MenB vaccine is immunogenic and safe in adults and infants

# Limitations of Conventional Approaches to Vaccinology for Prevention of MenB Disease

## • Capsular Approaches

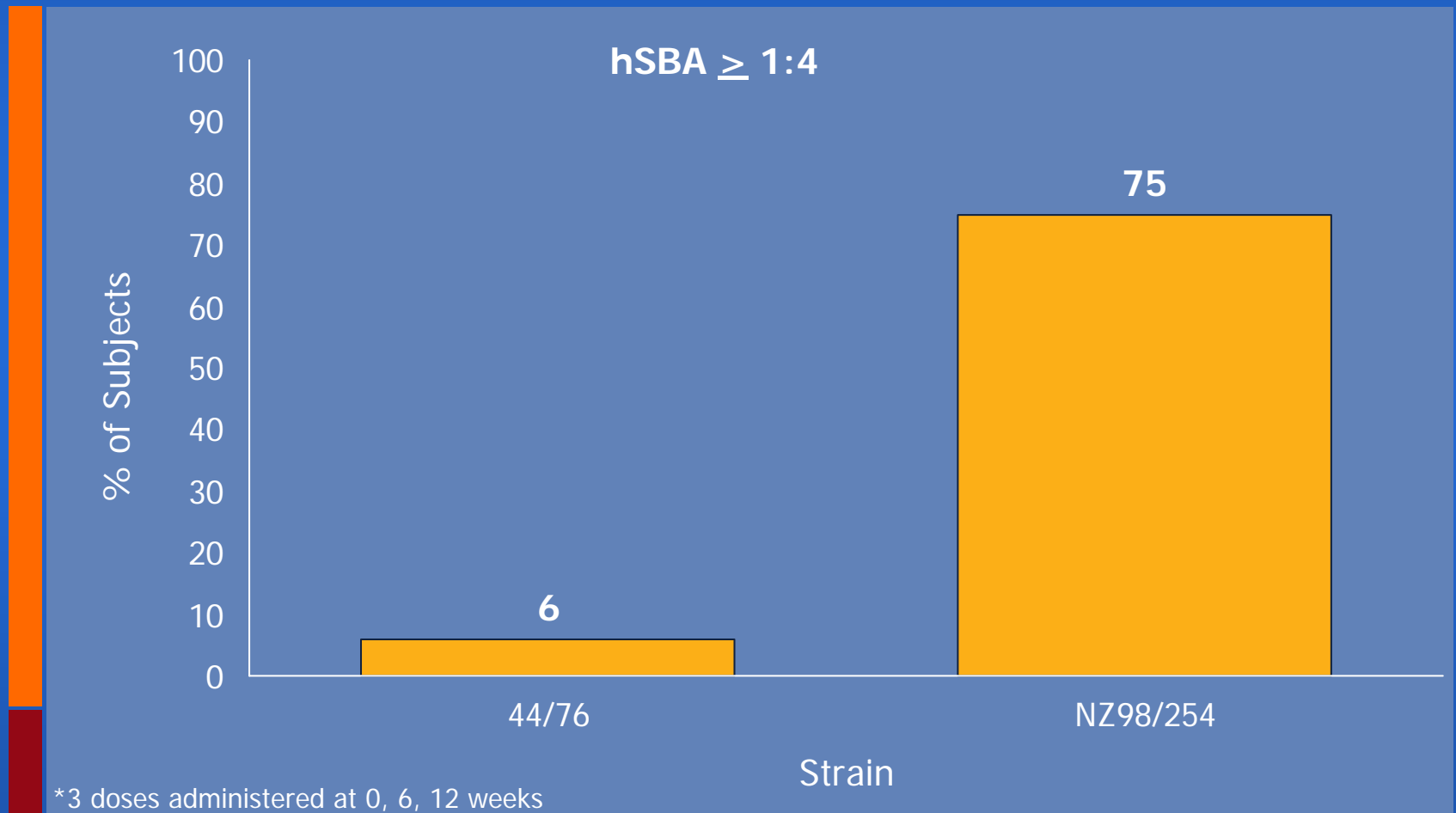
- Plain polysaccharide vaccines<sup>1,2</sup>
  - Poorly immunogenic
  - Risk of autoimmunity
- N-propionylated polysaccharide conjugates<sup>3</sup>
  - No functional activity of vaccine induced antibodies

## • Non-Capsular Approaches<sup>4</sup>

- OMV vaccines<sup>5,6</sup>
  - Sequence and antigen variability
  - Protection only against homologous strain
- With the exception of NspA, all the surface-exposed proteins described during the past 3 decades are limited by antigenic variability.<sup>7</sup>

# Immunogenicity MeNZB™ OMV Vaccine

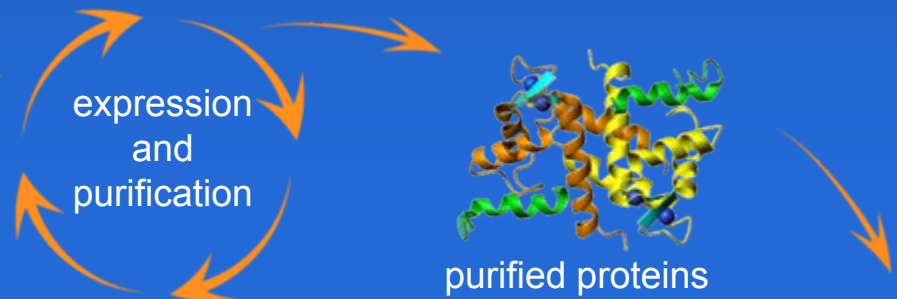
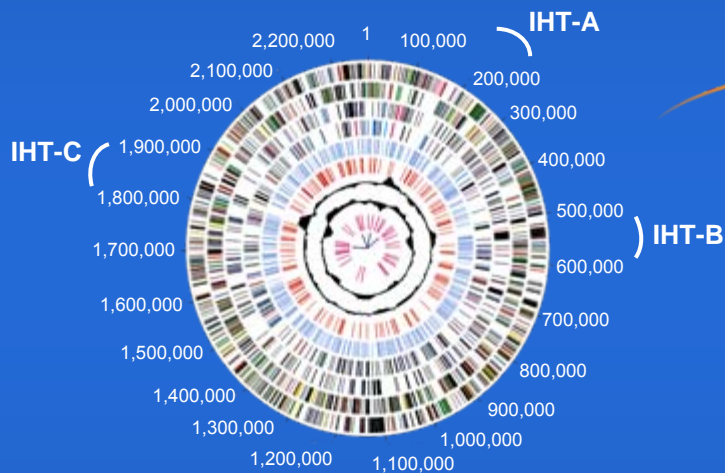
Phase II 16-24 month old toddlers: Post 3<sup>rd</sup> dose\*



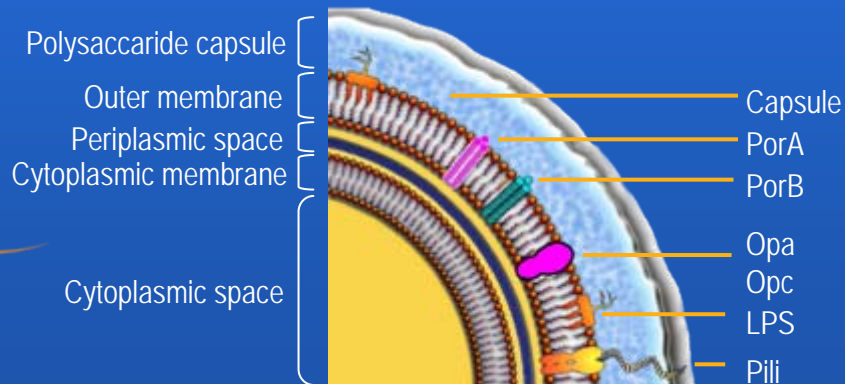
# Reverse Vaccinology Approach

Based on the genome sequence of MC58, **600** ORFs that potentially encoded novel surface exposed or exported proteins were identified

**~350** proteins successfully expressed in *E.coli*, purified, and used to immunize mice



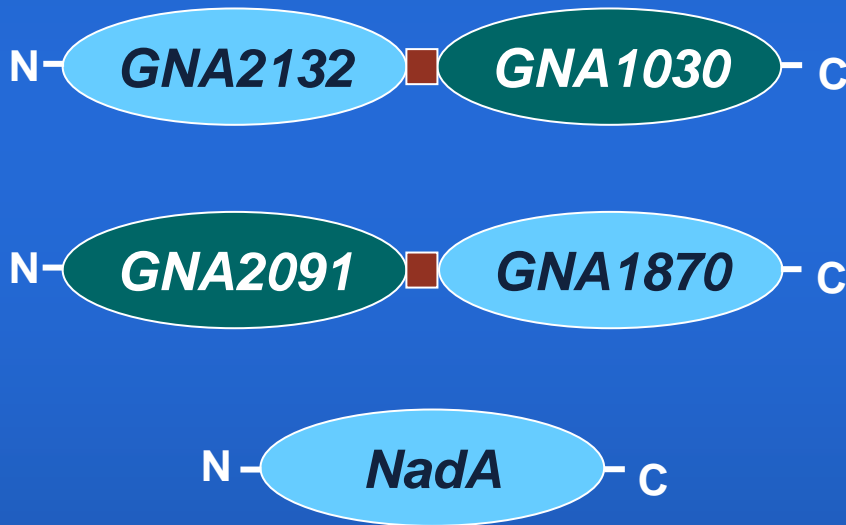
**91** novel surface-exposed proteins identified



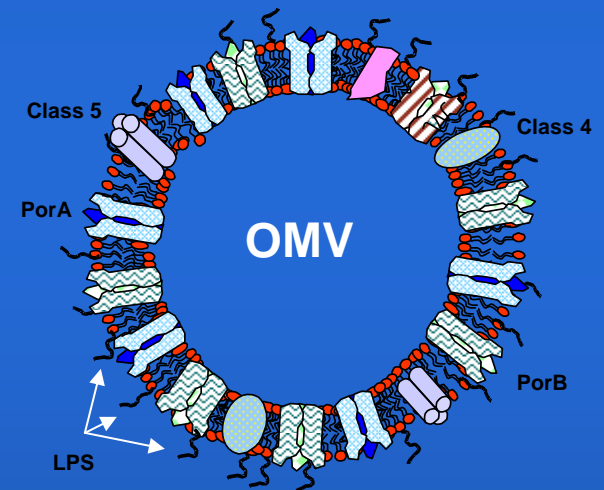
**28** novel protein antigens with bactericidal activity were identified

# Protein Antigen Combinations in an Effective Serogroup B Vaccine

3 protein antigens (2 fusion proteins and one single polypeptide)

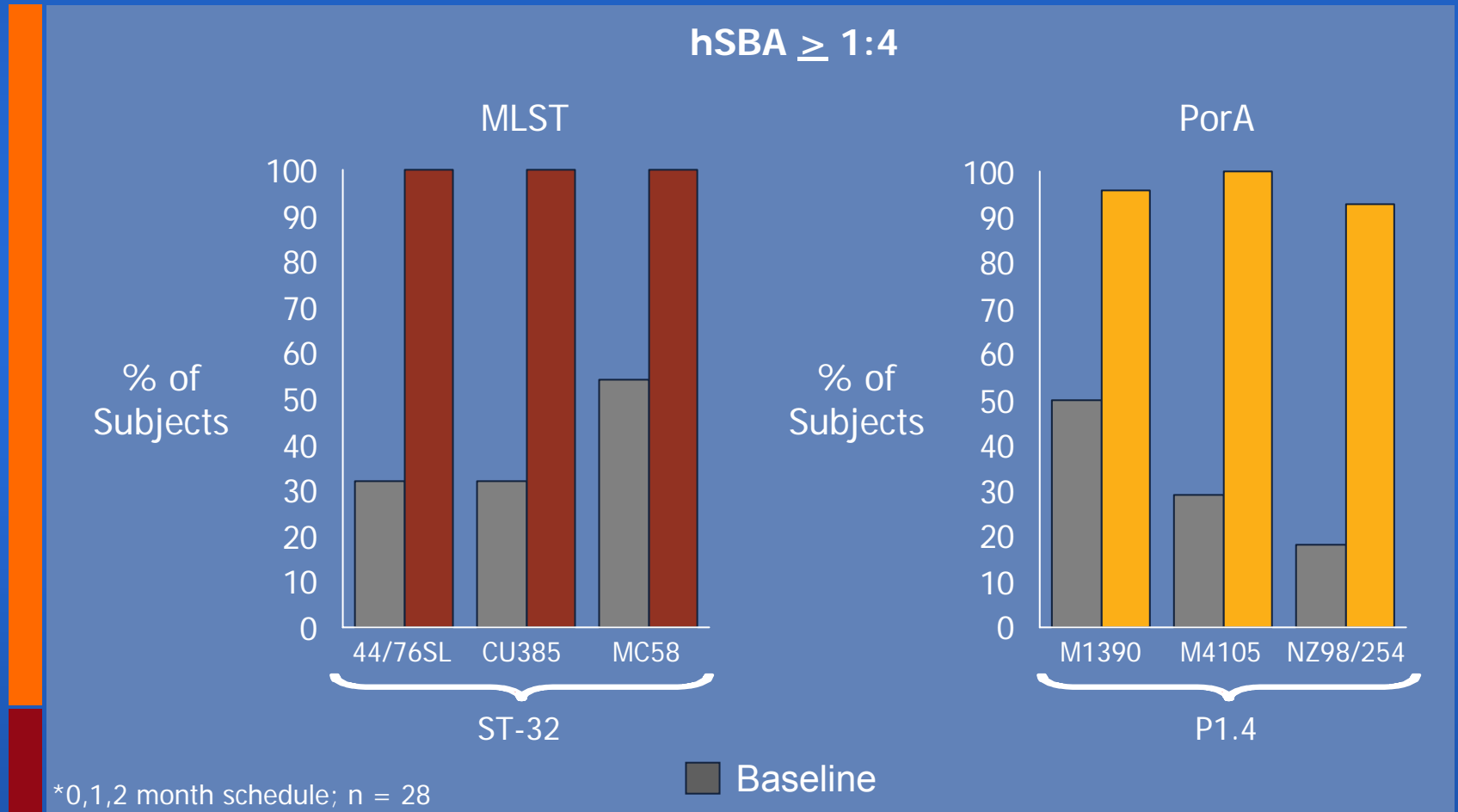


Outer Membrane Vesicle (OMV) component (NZ PorA is P1.4)



# Reverse Vaccinology: Proof of Concept

## Phase I Adults: 1-month post 3<sup>rd</sup> dose\*



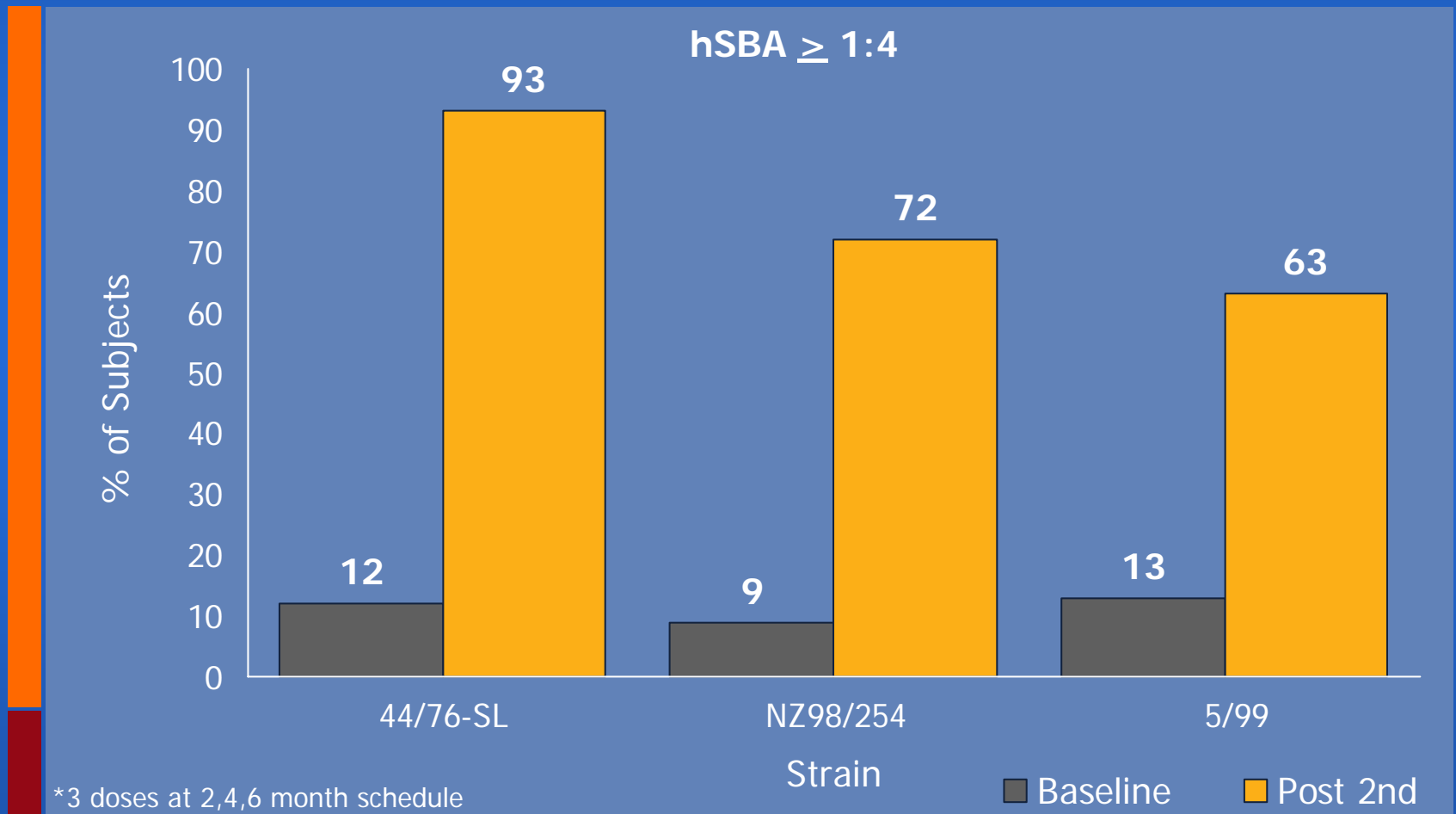
# Novartis MenB Vaccine Immunogenicity Results in Adults

Phase I Adults Study: Post 3<sup>rd</sup> dose\* for 3 reference strains



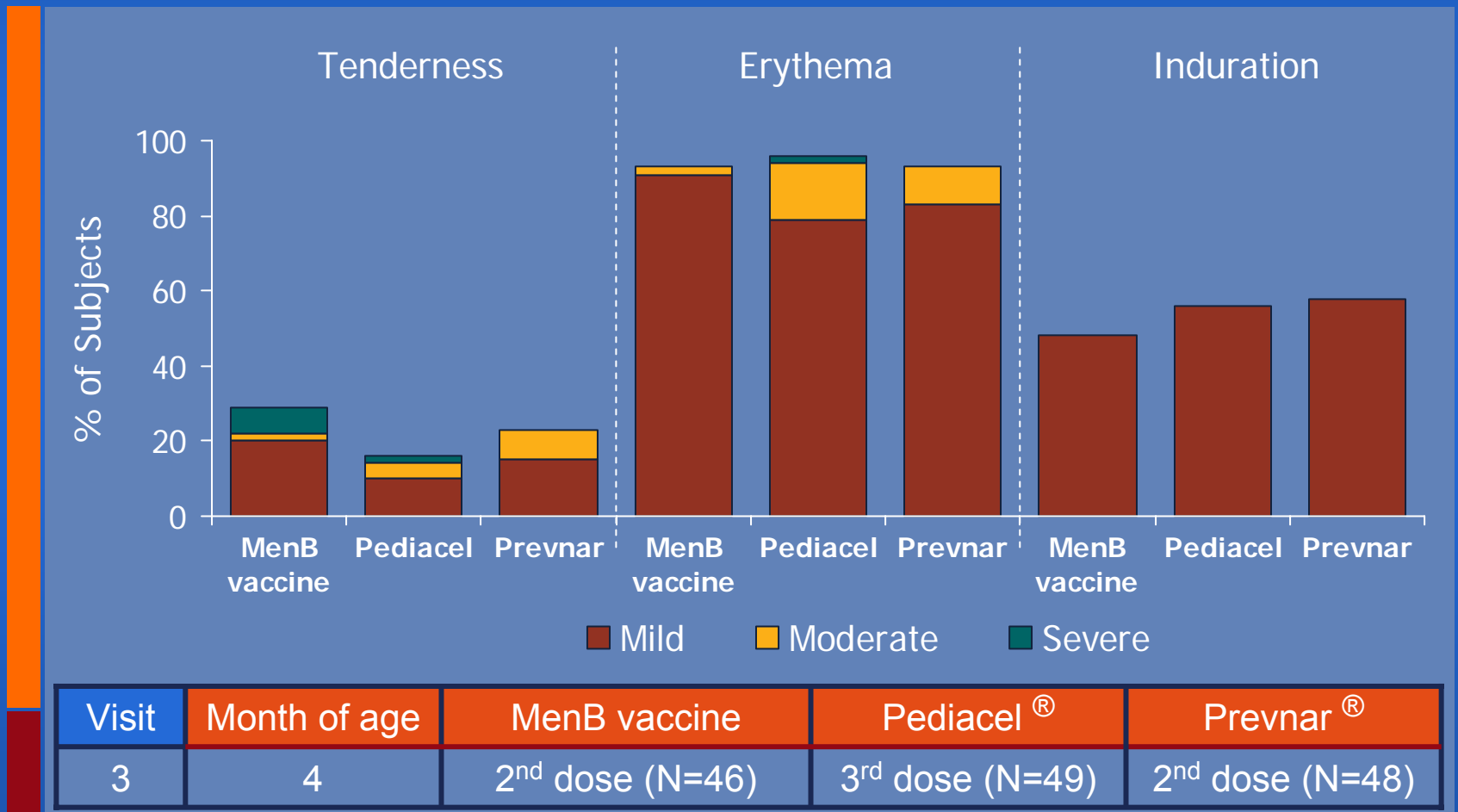
# Novartis MenB Vaccine Immunogenicity Results in Infants (*Interim Data*)

Phase II Infants Study UK: Post 2<sup>nd</sup> dose\* for 3 reference strains



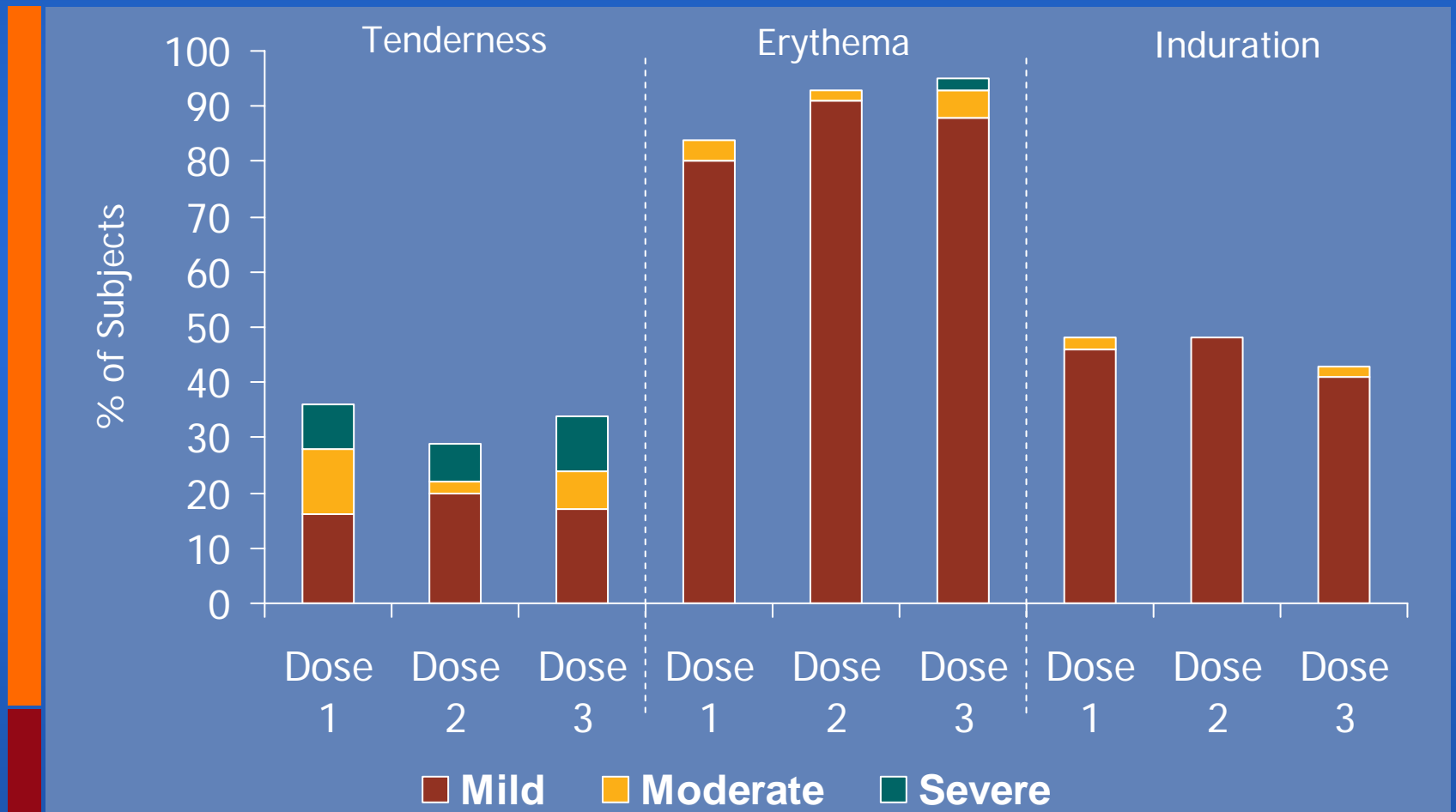
# Novartis MenB Vaccine Comparable Local Reactions (*Interim Data*)

## Phase II Infants Study UK: Post 2<sup>nd</sup> dose



# Novartis MenB Vaccine Local Reactions Post Each Dose *(Interim Data)*

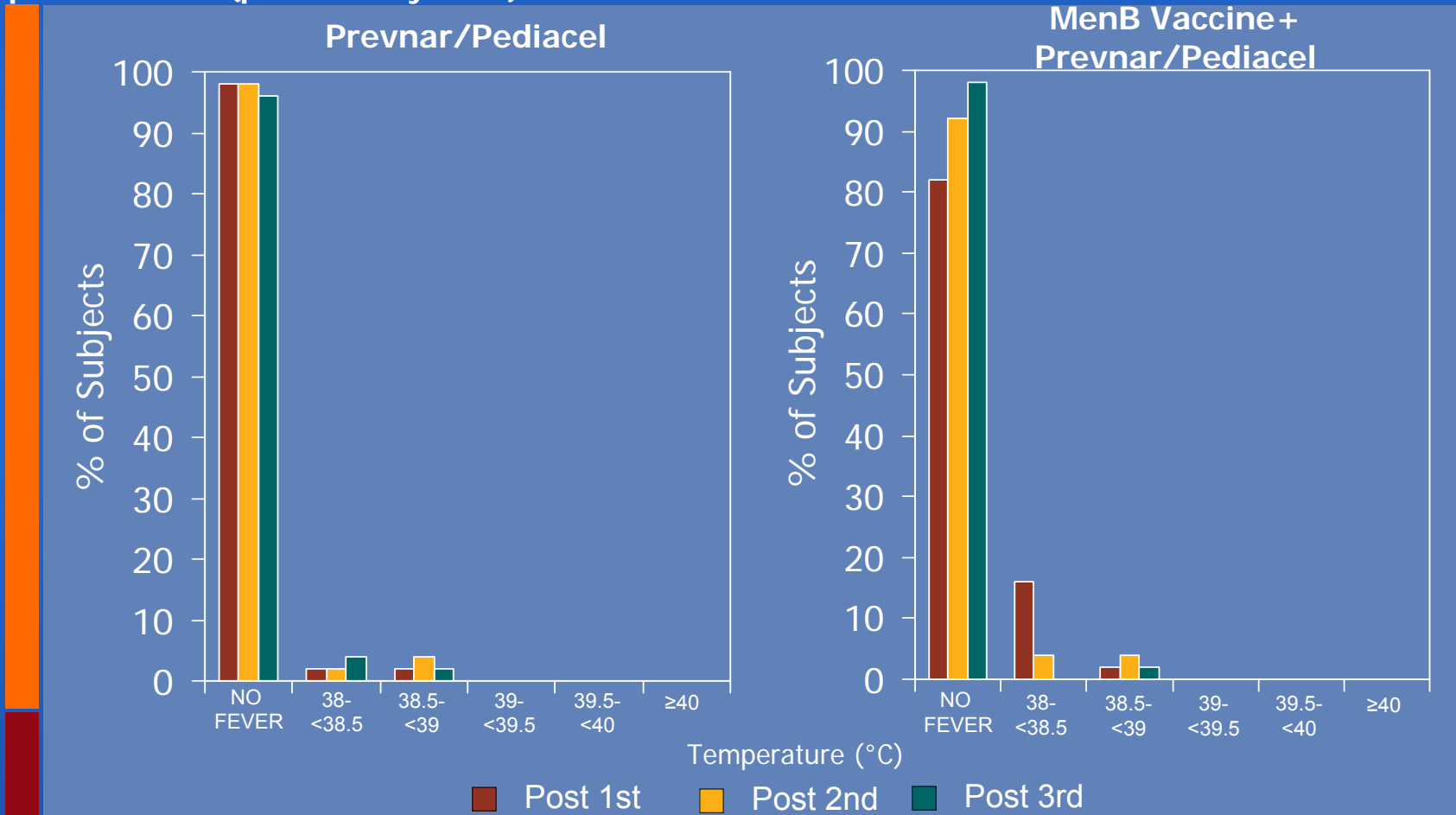
## Phase II Infants Study UK



# Novartis MenB Vaccine Systemic Reaction: Fever

## Phase II Infants Study UK (*Interim Data*)

More fever seen post 1<sup>st</sup> dose vs other routine vaccines, comparable post 2<sup>nd</sup> dose and post 3<sup>rd</sup> dose (preliminary data)\*



\*Fever data were collected within 48 hours of vaccination



# Summary

- *N. meningitidis* serogroup B
  - Highest incidence in many regions of the world
  - Causes outbreaks and is unpredictable
- Reverse vaccinology is an effective approach to identifying novel vaccine candidates against serogroup B
- Novartis MenB vaccine
  - Developed from the analysis of the meningococcal genome
  - Induces a robust bactericidal immune response
  - Immunogenic and safe in adults and infants
  - Vaccine moving into Phase III clinical trials
- The Novartis MenB vaccine is the first vaccine based on recombinant proteins to demonstrate bactericidal immune response in adults and infants



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