

LYMErix
Lyme Disease Vaccine (Recombinant OspA)

FDA Advisory Committee Meeting
Vaccines and Related Biological
Products

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LYMErix
Lyme Disease Vaccine (Recombinant OspA)

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GlaxoSmithKline**

AGENDA - LYMErix

- **Introduction and History** **Dr. Clare Kahn** **GSK US**
- **Theoretical Considerations
of Treatment-resistant
Lyme Arthritis** **Dr. Yves Lobet** **GSK Bio**
- **Safety Assessment
for Licensure** **Dr. Francois Meurice** **GSK Bio**
- **Safety Assessment
Post-Licensure** **Dr. Bernard Hoet** **GSK Bio**
- **Phase IV Post Marketing
Safety Study at HPHC** **Dr. Richard Platt** **HPHC**
- **Conclusion** **Dr. Clare Kahn** **GSK US**

Lyme Disease: Epidemiology

- **Lyme disease (LD) is a multisystem disease caused by infection with the spirochete *Borrelia burgdorferi* (*B. b.*), which is transmitted by Ixodes ticks**
- **Most commonly diagnosed vector-borne disease in the United States**
(> 100,000 cases reported to the CDC, 1982 to 1998)
- **Now a vaccine-preventable disease but still on the rise**

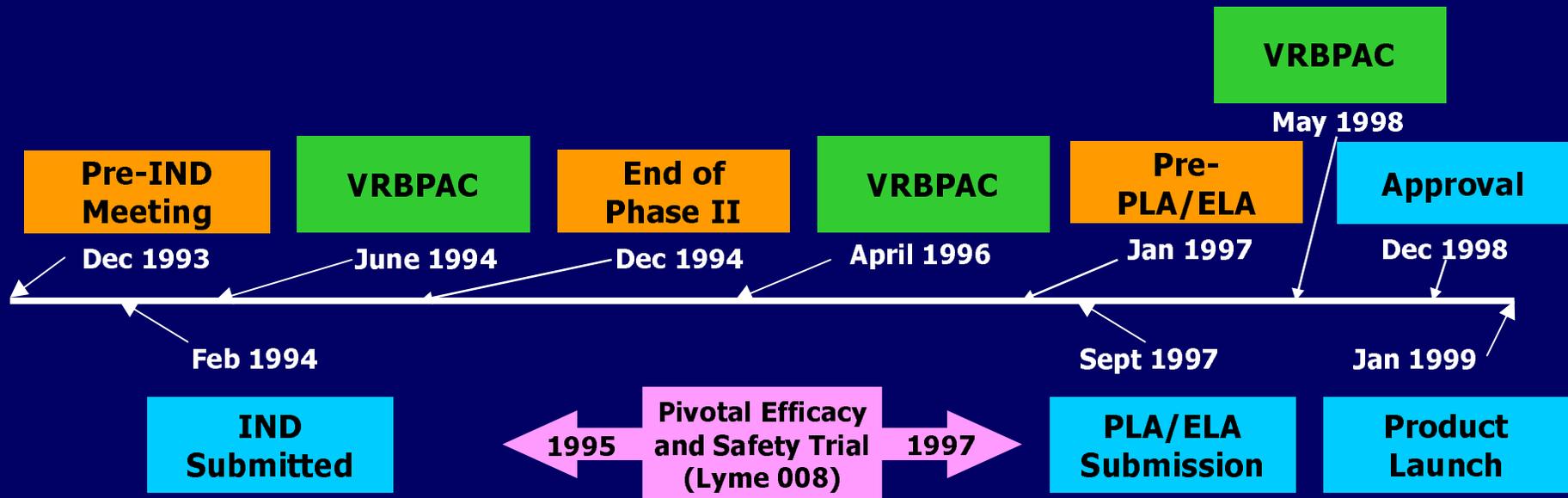
Lyme Disease: Manifestations

- **Early LD: rash (EM), fever, fatigue, myalgias, arthralgias**
- **Early Disseminated LD: 2° skin lesions, neurologic, cardiac involvement, musculoskeletal symptoms**
- **Late LD: chronic arthritis, neurologic abnormalities or acrodermatitis chronica atrophicans; sometimes permanent sequelae.**

LYMErix Vaccine

- **Noninfectious recombinant vaccine developed and manufactured by SB Bio (GSK Bio)**
- **Contains Lipo-OspA, an outer surface protein of *B. b. sensu stricto* ZS7, as expressed by *Escherichia coli***
- **Each 0.5 mL dose contains 30 mcg Lipo-OspA adsorbed onto 0.5 mg Al**
- **Primary immunization against LD consists of three doses of LYMErix given i.m. at 0, 1 and 12 months in individuals 15-70 years of age**

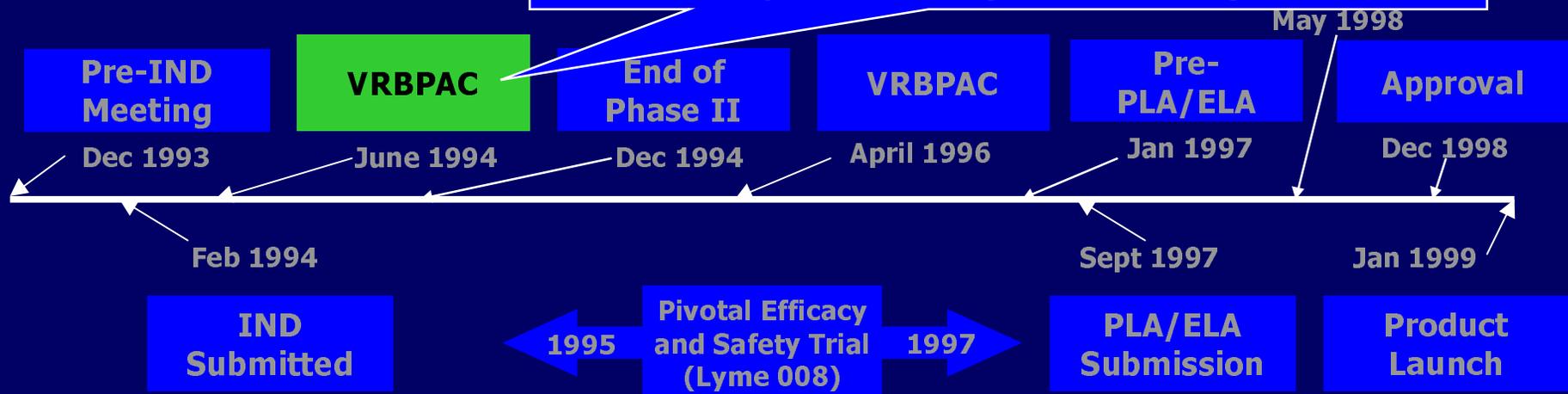
Regulatory History



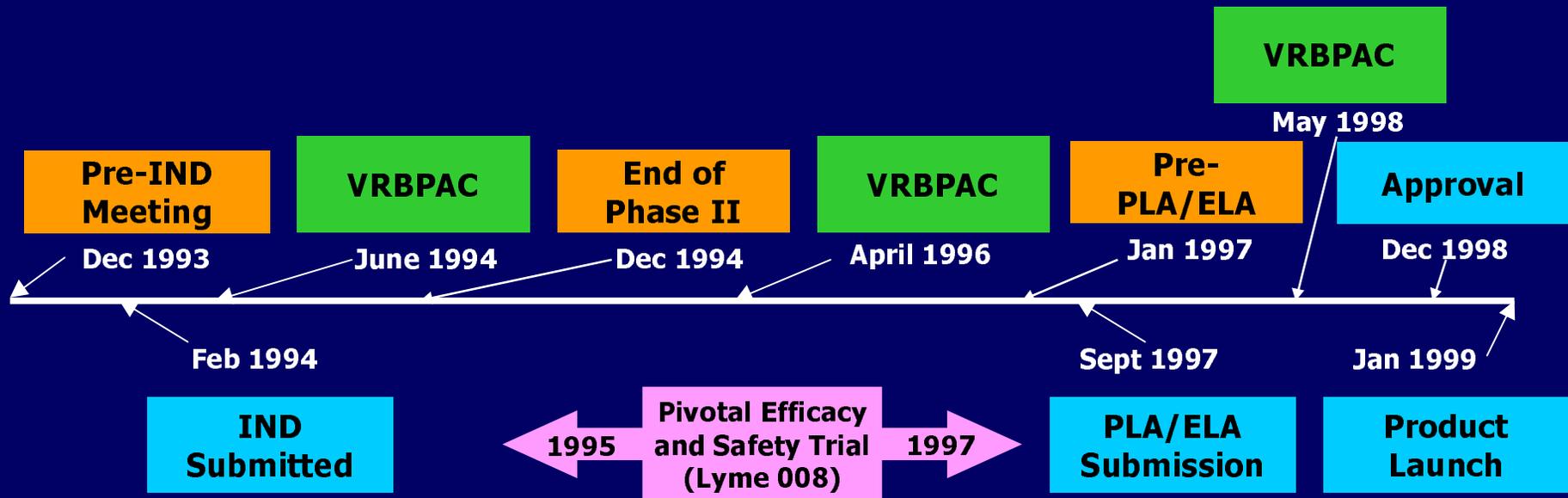
Regulatory History

**Review of Lyme Disease
Recommendations for Pivotal Development of Vaccines:**

- LD case definition
- 1^o and 2^o pivotal study endpoints
- two-year follow-up for safety and efficacy
- inclusion of patients with previous history of LD.



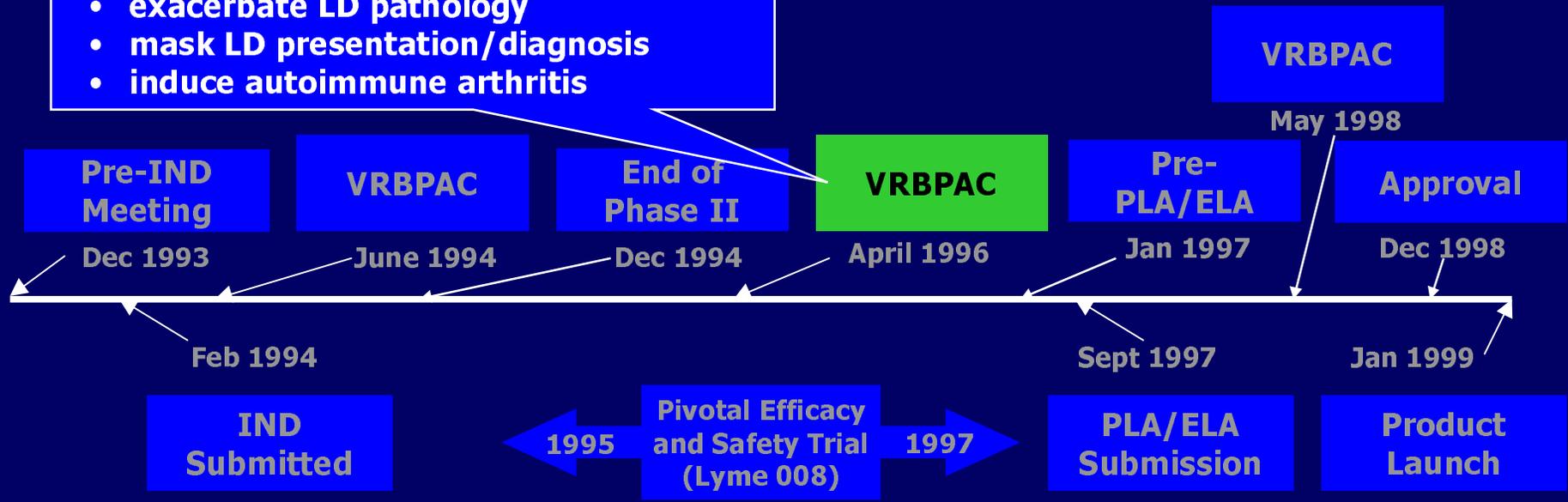
Regulatory History



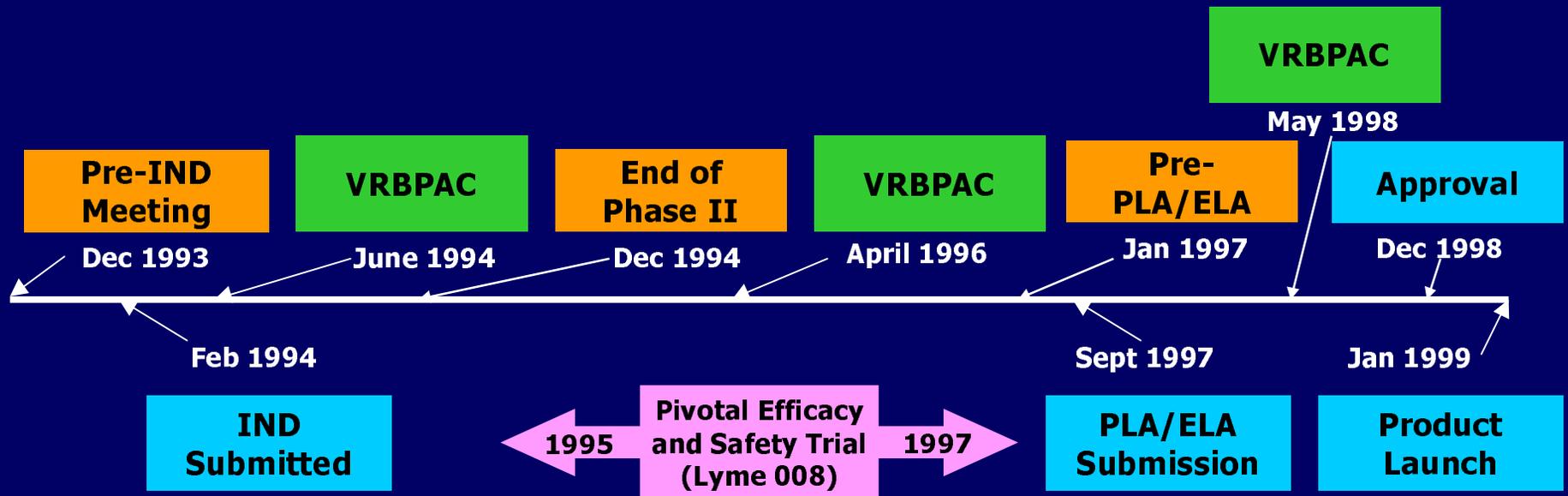
Regulatory History

Pediatric Development
Theoretical Safety Considerations i.e. potential for L-OspA vaccine to:

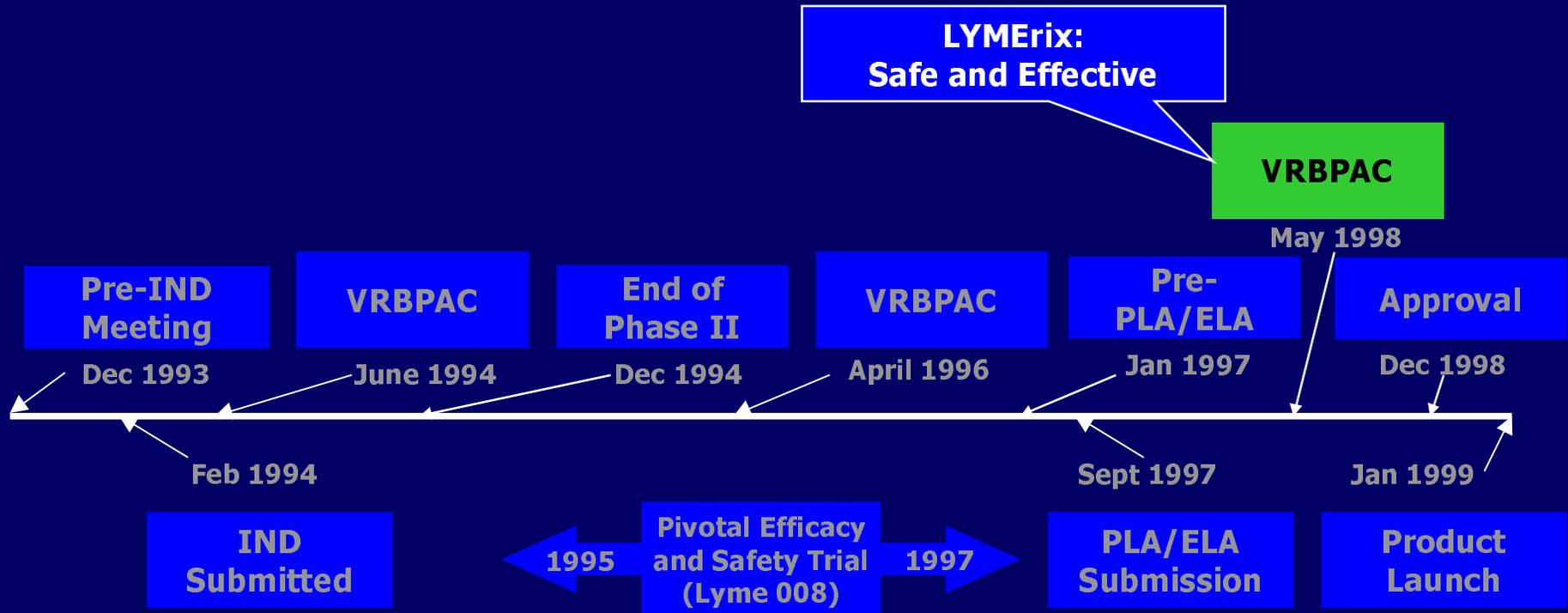
- exacerbate LD pathology
- mask LD presentation/diagnosis
- induce autoimmune arthritis



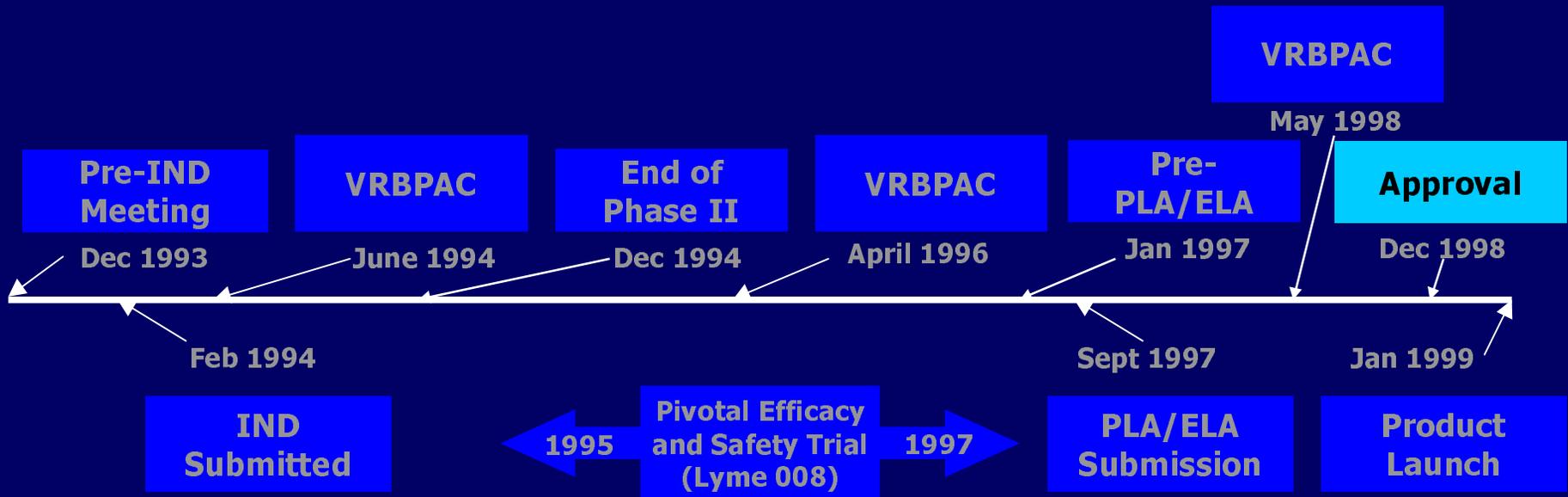
Regulatory History



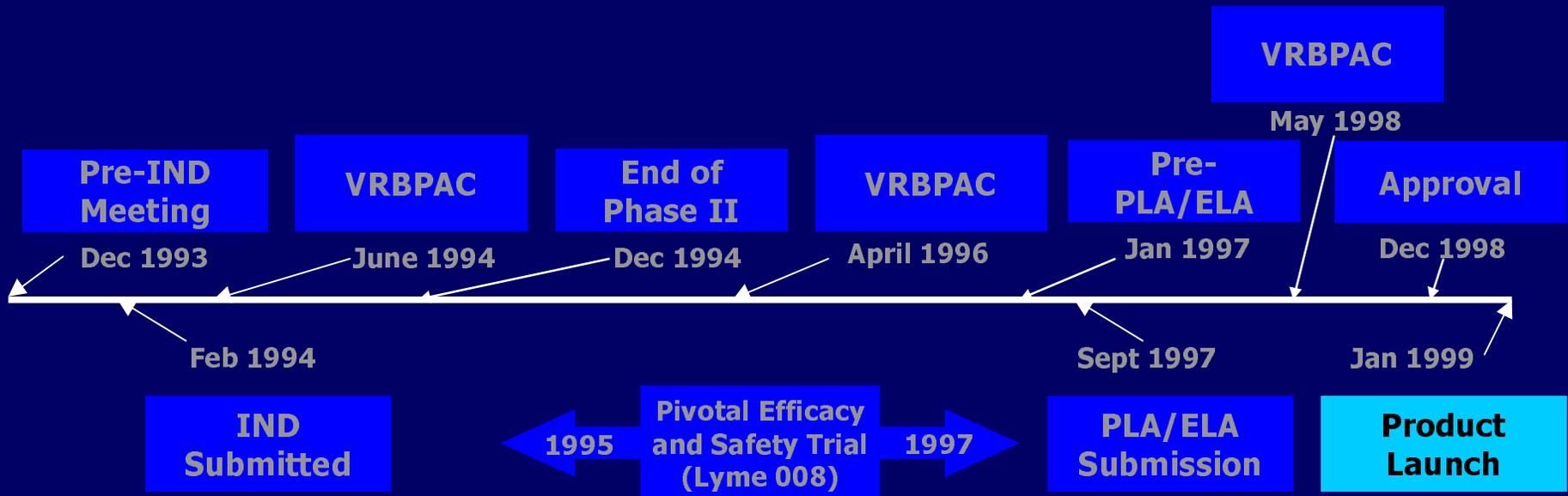
Regulatory History



Regulatory History



Regulatory History



Regulatory History: Post Licensure Commitments

- **Phase IV post marketing cohort safety study initiated** **January 2000**
 - **3 Quarterly Reports submitted indicate low uptake at HPHC** **2000**
- **Study on cell mediated immunity (Lyme 008 subset) - submitted** **December 1999**
- **Safety assessment pertaining to those of childbearing potential**
 - **Reprotoxicity study in animals report submitted** **January 2000**
 - **Establish pregnancy registry** **In Effect**

Regulatory History: Postmarketing Surveillance

- **Additional Timeliness:**

- expedition of reports of musculoskeletal and neurological events within 15 days regardless of seriousness

June 2000

- **Ensure Maximal Capture:**

- GSK Letter to investigators of completed and ongoing clinical trials, reinforcing for them requirements for reviewing and reporting adverse events

November 2000

Regulatory History: Postmarketing Experience to Date

- **Most frequently reported AEs involve reactogenicity with symptoms already described in the product label.**
 - **These reports allow us to identify that, in certain individuals, these symptoms are described as occurring concomitantly.**
- **Hypersensitivity has also been reported.**

Conclusions

- **LD is now a vaccine-preventable disease still on the rise**
- **LD associated with chronic morbidities sometimes with permanent sequelae**
- **Collaborations with CBER and VRBPAC (1993-1998) guided Lyme vaccine through development to licensure**
- **To date, available data from PM surveillance, PM commitments and additional clinical trials are in keeping with the pre-licensure safety profile**