BAVARIAN NORDIC

Current State of Research Development & Stockpiling of Smallpox Medical Countermeasures

National Academies

14 December 2023

Traditional Smallpox Vaccines Eradicated Smallpox but are Associated with Rare Serious Side Effects

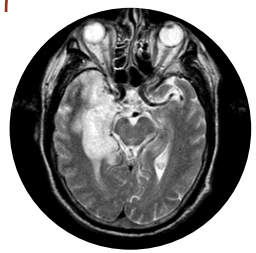
- Based on replicating vaccinia virus strains
- Administered using a special bifurcated needle
- Cause a “vaccine take” – only historical measure of efficacy (protection)
- Eradicated smallpox in 1980

FDA warning label for ACAM2000 (8/2007)

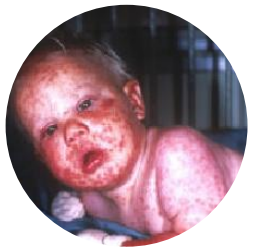
WARNING:

See full prescribing information for complete boxed warning

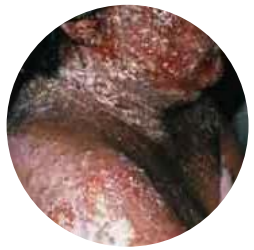
- **Myocarditis and pericarditis (suspect cases observed at a rate of 5.7 per 1000 primary vaccinees (95% CI: 1.9-13.3)), encephalitis, encephalomyelitis, encephalopathy, progressive vaccinia, generalized vaccinia, severe vaccinial skin infections, erythema multiforme major (including STEVENS-JOHNSON SYNDROME), eczema vaccinatum resulting in permanent sequelae or death, ocular complications and blindness and fetal death, have occurred following either primary vaccination or revaccination with live vaccinia virus smallpox vaccines. These risks are increased in certain individuals and may result in severe disability, permanent neurological sequelae and/or death [see Warnings and Precautions (5)].**



Post-vaccinal Encephalitis

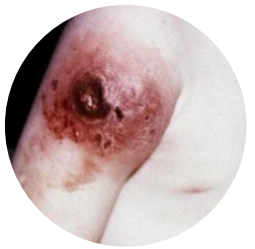


Generalized Vaccinia Infection

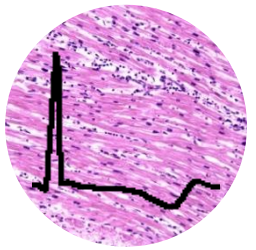


Eczema vaccinatum

Autoinoculation



Progressive Vaccinia



Myo-pericarditis

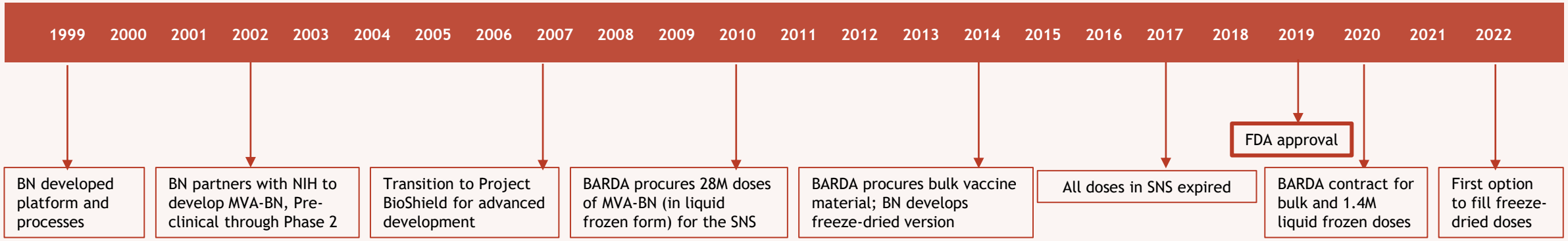
BAVARIAN NORDIC

USG/BN partnership to develop JYNNEOS

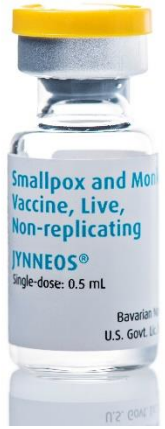
- BN initiated MVA-BN smallpox program in early 2000s
  - Developed proprietary MVA platform technology
  - Conducted the first clinical trial in Germany

- USG and BN collaboration initiated in 2002 to develop a smallpox vaccine for the general population and for people with weakened immune systems.
- FDA approved JYNNEOS in 2019 for adults determined to be at high risk for smallpox or monkeypox infection.
- BARDA procured JYNNEOS through Project BioShield for the Strategic National Stockpile.
- BN ultimately manufactured ¬40M doses for USG since beginning of program

JYNNEOS development pathway



JYNNEOS Approved by FDA



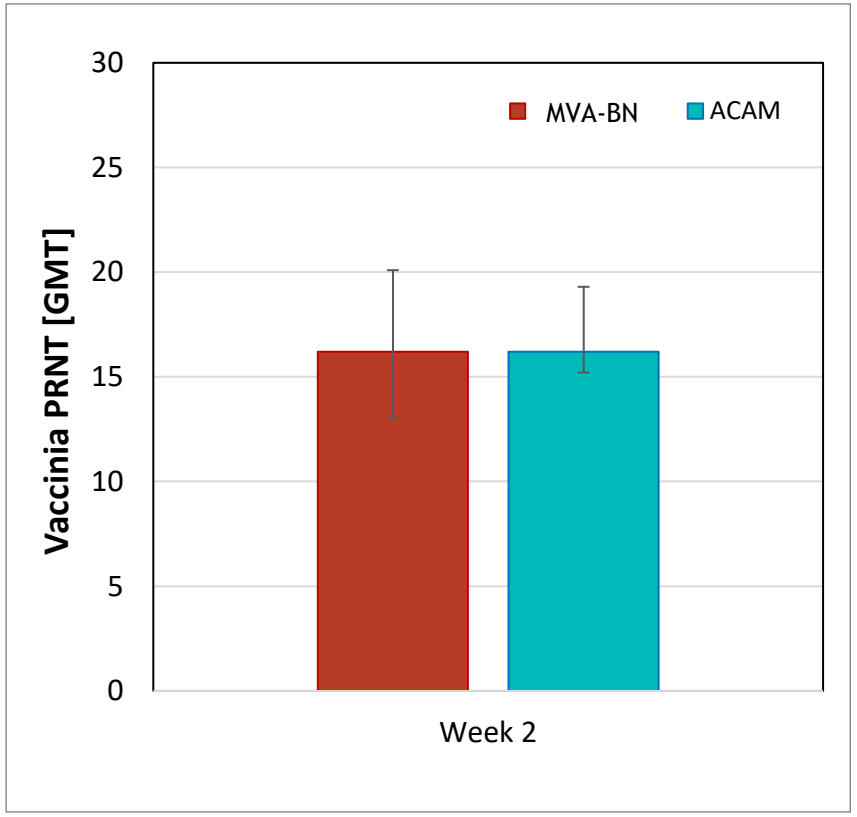
- JYNNEOS (Smallpox and Monkeypox Vaccine, Live, Nonreplicating) is a live vaccine produced from the strain MVA-BN, an attenuated, **non-replicating** orthopoxvirus.
- **JYNNEOS is indicated for prevention of smallpox and monkeypox** disease in adults 18 years of age and older determined to be at high risk for smallpox or monkeypox infection
- Vaccine effectiveness against smallpox was inferred by comparing immunogenicity of JYNNEOS to a licensed smallpox vaccine (ACAM2000and was supported by efficacy data from animal studies.
- Standard dose regimen: Subcutaneous injection of **two doses four weeks apart**, for all populations, including vaccinia-experienced.
- **No contraindications** in the label, but precautions for individuals with known, previous severe allergic reactions to any of the components of JYNNEOS.

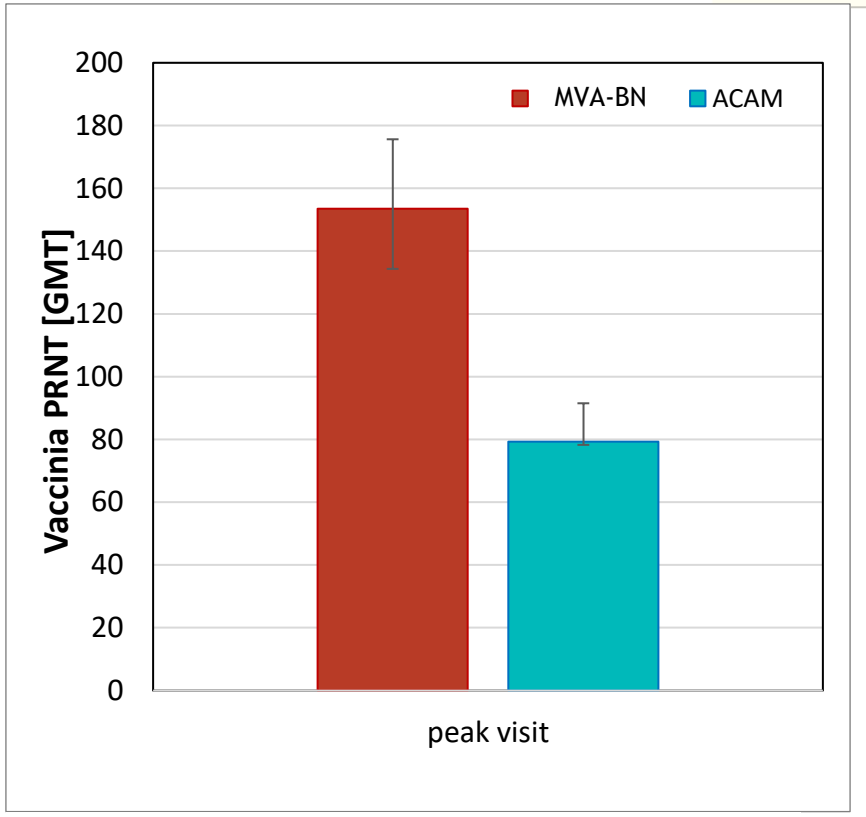
BAVARIAN NORDIC

MVA-BN also approved in EU (IMVANEX) and Canada (IMVAMUNE)

Phase 3 Immune Response Data

MVA-BN induced non-inferior immune response compared to ACAM2000





Primary Immunogenicity Endpoint

The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 NOVEMBER 14, 2019 VOL. 381 NO. 20

Phase 3 Efficacy Trial of Modified Vaccinia Ankara as a Vaccine against Smallpox

Phillip R. Pittman, M.D., Matthew Hahn, M.D., HeeChoon S. Lee, M.D., Craig Koca, M.D., Nathaly Samy, M.D., Darja Schmidt, Ph.D., Joachim Hornung, Heinz Weidenthaler, M.D., Christopher R. Heery, M.D., Thomas P.H. Meyer, Ph.D., Günter Silbernagl, M.Sc., Jane Maclennan, B.Sc., and Paul Chaplin, Ph.D.

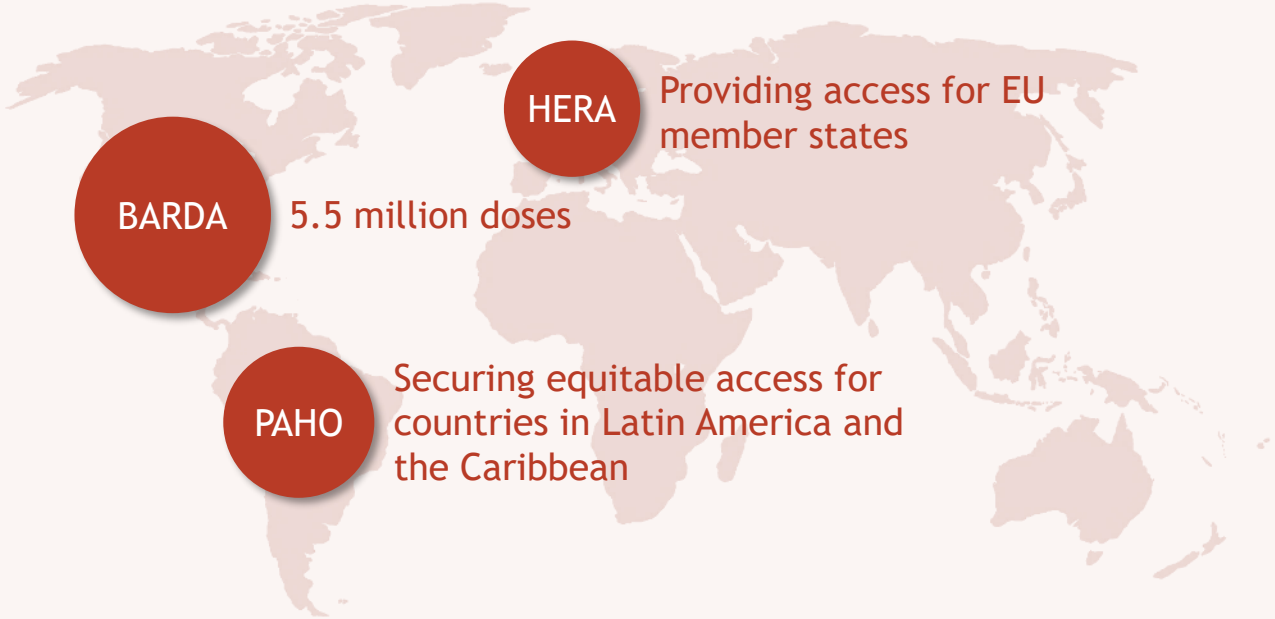
ABSTRACT

Requirement to demonstrate **non-inferiority (NI)** of MVA-BN to ACAM in PRNT (peak visit):
the lower (two-sided) 95% CI limit of the GMT ratio (MVA-BN/ACAM) is above 0.5 (predefined NI margin).

Vaccinations: MVA-BN (week 0, week 4), ACAM (week 0)

BAVARIAN NORDIC

Our response to the global mpox outbreak



More than 70 countries across the Americas, Europe, Asia and Oceania have access to MVA-BN

BAVARIAN NORDIC

Pre-mpox outbreak status:

- USG had 15 million dose equivalents in stock as bulk and 1.4 million filled doses available
- No bulk production ongoing/planned and filling line running at 1 batch/week

4M doses
supplied globally by end of 2022

15M doses
supplied globally by end of 2023

of which
5.5M doses
supplied in response to BARDA orders

Proven Effectiveness of JYNNEOS to Prevent Mpox Disease & Hospitalizations

- JYNNEOS has played a crucial role in controlling 2022 mpox outbreak - at least 1.8 million doses administered
- A systematic literature review (SLR) performed summarising the evidence on Vaccine Effectiveness (VE) from 13 studies (Jan 2022 to Nov 23)
- SLR assessed the strengths and limitations of each study - despite significant heterogeneity in study design and at-risk population definitions, the findings from the totality of the data were largely consistent and reflect strong effectiveness of MVA-BN at preventing symptomatic mpox disease.
- In 12 observational studies conducted in vaccine-eligible individuals (according to local recommendations), adjusted VE estimates ranged from **66 to 90% after two doses** and from **36 to 89% after 1 dose**.
- In a surveillance study conducted from in the US, MVA-BN was shown to reduce the risks of mpox-related hospitalisation - Compared with unvaccinated mpox patients, vaccinated individuals had **73% hospitalisation risk reduction after one dose**, and **80% after two doses**

BAVARIAN NORDIC

Lessons Learnt from Mpox Outbreak

- Vaccine safety matters – even in an outbreak situation
  - Hesitancy / refusal to use 1st & 2nd generation smallpox vaccines

- Governments with JYNNEOS stockpiles were better prepared
  - BN's bulk inventory allowed JYNNEOS supply during 2022

- USG invested 30 billion USD in the development and procurement of COVID vaccines
  - There were no vaccines. Required rapid development and backing of numerous vaccine candidates.

- For Mpox there was a safe and effective vaccine available due to the development of JYNNEOS – USG/BN partnership
  - Investment (¬2 billion USD) in a solution for a specific threat (smallpox) and emerging disease (Mpox) meant there was a vaccine on stock and a manufacturing supply able to met the outbreak

BAVARIAN NORDIC

JYNNEOS Summary

- JYNNEOS was developed through a highly successful partnership between USG and BN
- Approved in 2019 against smallpox and mpox and stockpiled in the SNS
- Rapidly deployed within the US and 15 million doses distributed Worldwide to more than 70 countries – supply available due to USG/BN partnership
- JYNNEOS has shown to be a highly effective vaccine against Mpox
  - Single shot shown to have a high efficacy allowing a delay in the booster should vaccine supplies be low
- A highly successful model to develop an effective vaccine against an identified National threat (Smallpox) and an emerging disease (Mpox)

BAVARIAN NORDIC


BAVARIAN NORDIC