US FDA approves TPOXX (tecovirimat) first ever drug with an indication for treatment of smallpox approved on 13th July 2018

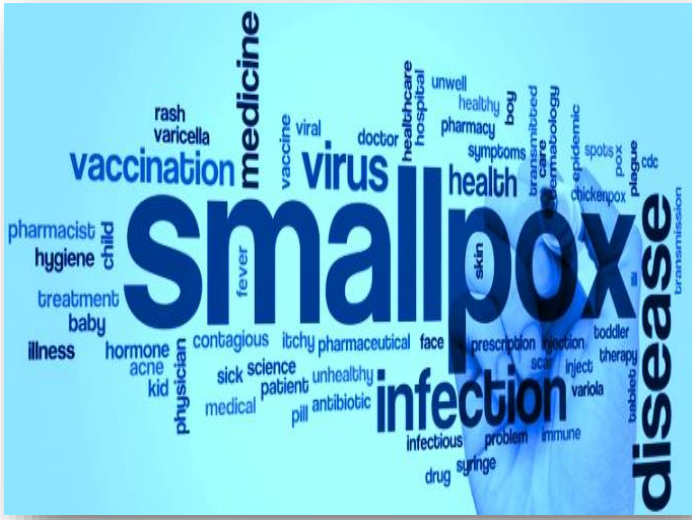
SIGA

Human BioArmor

FDA approves the first drug with an indication for treatment of smallpox

TPOXX

Oral Tecovirimat for the Treatment of Smallpox



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About TPOXX (tecovirimat) -1

About the SIGA Technologies

- SIGA Technologies, Inc. is a pharmaceutical company set up in 1995 that is now based in New York City. SIGA lead product is TPOXX® (USAN tecovirimat, ST-246®) an orally administered antiviral drug that targets orthopoxvirus infections. While TPOXX is not yet approved as safe or effective by the U.S. Food & Drug Administration, it is a novel small-molecule drug that is being delivered to the U.S. Strategic National Stockpile ("SNS") under the Project BioShield Act of 2004 ("Project BioShield").
- TPOXX has been approved by the FDA for the treatment of human smallpox disease. On May 13, 2011, SIGA signed a contract with the Biomedical Advanced Research and Development Authority (BARDA) of the U.S. Department of Health and Human Services (the "BARDA Contract") pursuant to which SIGA agreed to deliver two million courses of TPOXX to the Strategic National Stockpile ("SNS"). The BARDA Contract is worth approximately $472 million, including $409.8 million for the manufacture and delivery of 1.7 million courses of TPOXX (an additional 300,000 courses are being delivered to the SNS at no charge) and $62 million of potential reimbursements (the "Base Contract"). In addition to the Base Contract, the BARDA Contract also contains various options that are exercisable at BARDA's discretion.

Brief on TPOXX

- TPOXX is an inhibitor of the orthopoxvirus VP37 envelope wrapping protein and is indicated for the treatment of human smallpox disease in adults and pediatric patients weighing at least 13 kg.
- **Limitations of Use:** The effectiveness of TPOXX for treatment of smallpox disease has not been determined in humans because adequate and well-controlled field trials have not been feasible, and inducing smallpox disease in humans to study the drug's efficacy is not ethical.

-TPOXX efficacy may be reduced in immunocompromised patients based on studies demonstrating reduced efficacy in immunocompromised animal models.

Source https://www.siga.com/
https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/208627s000lbl.pdf

About TPOXX (tecovirimat) - 2

Product information

. TPOXX (tecovirimat) capsules for oral use .

. DOSAGE AND ADMINISTRATION:

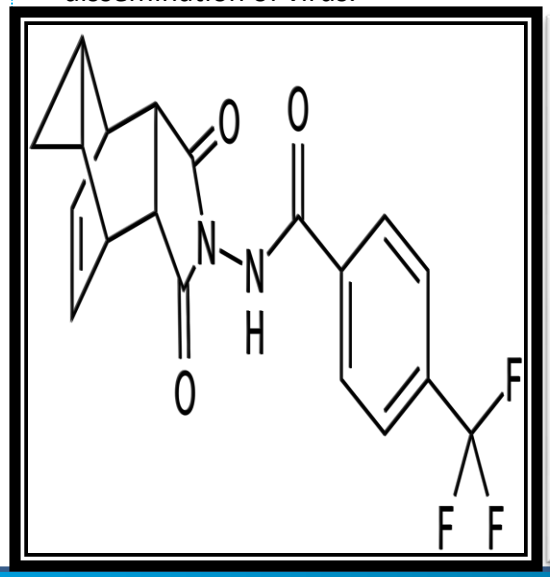
- **Capsule:** 200 mg.
- TPOXX should be taken within 30 minutes after a full meal of moderate or high fat.
- **Adults:** 600 mg twice daily for 14 days
- **Pediatrics patients weighing 13 kg or more :**

- 13 kg to less than 25 kg: 200 mg of TPOXX twice daily for 14 days
- 25 kg to less than 40 kg: 400 mg of TPOXX twice daily for 14 days
- 40kg or more: 600 mg of TPOXX twice daily for 14 days

- **CONTRAINDICATIONS:** None.
- **WARNINGS:** Hypoglycemia; Co-administration with Repaglinide.
- **Adverse Reactions:** Common adverse reactions in healthy adult subjects (≥ 2%) were headache, nausea, abdominal pain, and vomiting.

Mechanism of action

Tecovirimat targets and inhibits the activity of the orthopoxvirus VP37 protein (encoded by and highly conserved in all members of the orthopoxvirus genus) and blocks its interaction with cellular Rab9 GTPase and TIP47, which prevents the formation of egress-competent enveloped virions necessary for cell-to-cell and long-range dissemination of virus.



ST-246® (Tecovirimat) Product Profile

- Antiviral for post-event prophylaxis, treatment of symptomatic individuals
- Small molecule enables increased cost effectiveness and convenience
- Phase II trials completed; safe and well tolerated; pivotal trial to begin soon

Only Smallpox Antiviral to Demonstrate Efficacy in Non-Human Primate Models

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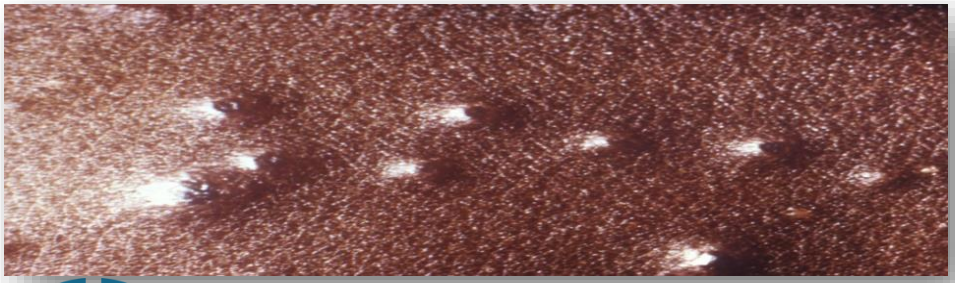
Source : https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/208627s000lbl.pdf

Smallpox Disease Burden

What is Smallpox?

- An eradicated virus that used to be contagious, disfiguring and often deadly.
- **Signs and Symptoms: Fever** is the most common initial symptom and can be quite high. This is accompanied by body aches , chills and headache. Often, the patient is too unwell to get out of bed (malaise). Within 24-48 hours, a rash begins to appear everywhere on the body but especially on the legs, arms, mouth, and face. **Pharyngitis** (sore throat abdominal pain, back pain) and occasionally vomiting may also develop.
- After one to two weeks, the lesions scab over and eventually fall off, leaving deep scars



Facts and Figures (1)

- The majority of patients with smallpox recover, but death occurs in up to 30% of cases.
- **1950s -** Worldwide, 15 million cases of smallpox are reported each year in the decade; the highly contagious disease kills more than 500 million people worldwide over the last century.
- **1977 -** The last naturally occurring case of smallpox in the world occurs in Somalia.
- **1979 -** Smallpox meets the criteria for eradication by having no natural cases for two years. There are two sanctioned repositories for stocks of variola, the virus that causes smallpox. They are: the Centers for Disease Control and Prevention in Atlanta and the Russian State Research Center of Virology and Biotechnology in Koltsovo.
- **1980 -** The World Health Organization announces the official eradication of smallpox.
- **2008 -** According to a study published in the American Journal of Medicine," researchers found that lifetime protection is obtained from just one vaccination, even when that vaccination occurred as much as 88 years ago."

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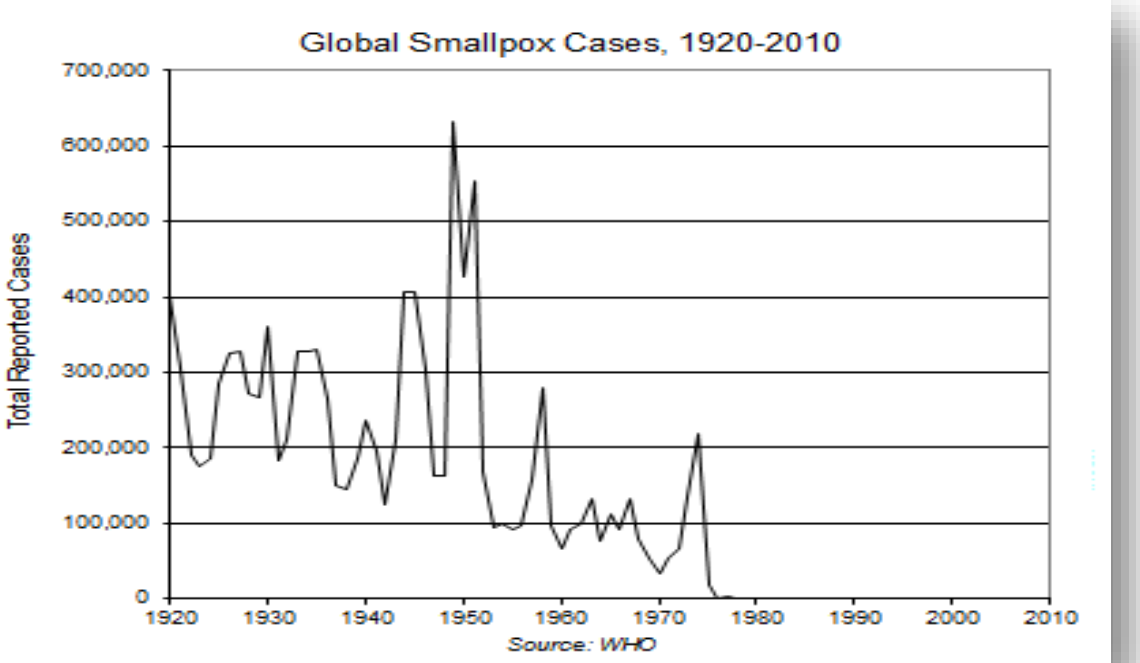
Source: https://www.google.com/search?newwindow=1&safe=active&source=hp&ei=J4JNW7PXOsLe9QOiuJrQDQ&q=smallpox&oq=smallpox&gs_l=psy-ab.3..0j0i131k1j0l8.2773.5782.0.6488.10.9.0.0.0.0.297.1463.0j3j4.8.0....0...1.1.64.psy-ab..2.7.1459.0...128.UZb1q0p_EFk

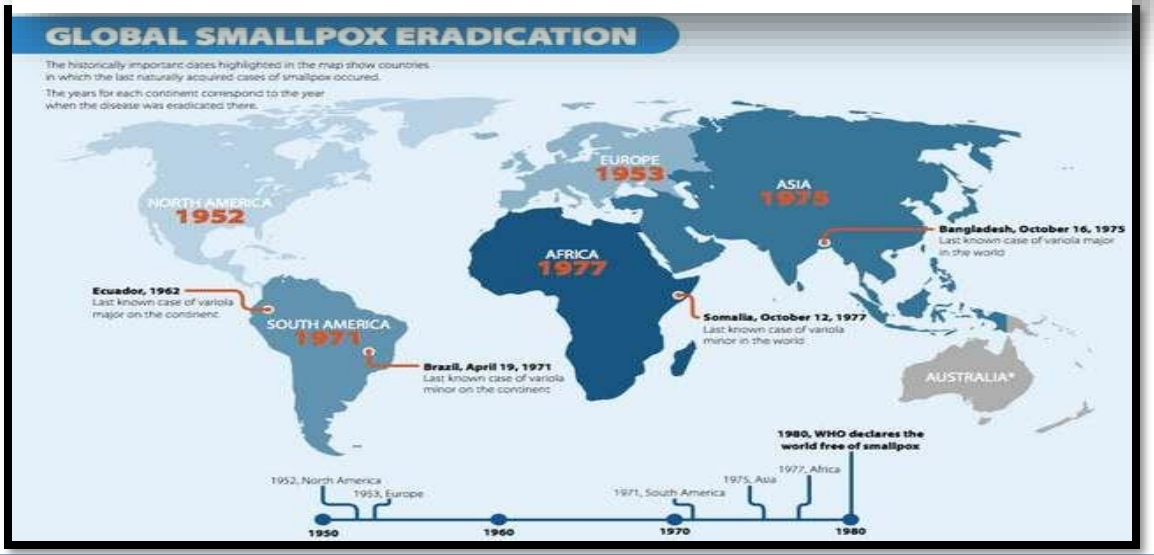
https://www.medicinenet.com/smallpox/article.htm

https://edition.cnn.com/2013/09/02/health/smallpox-fast-facts/index.html

Facts and Figures (2)

- **2014 -** Six vials containing the smallpox virus are found in an unused storage room at the Food and Drug Administration's Bethesda, Maryland, campus. Later testing shows that at least two of the vials, dating from 1954, contain the live virus.
- **2016 -** The oldest known sample of the smallpox-causing variola virus is found within the DNA of a 17th century child mummy in a crypt beneath a Lithuanian church, according to a study in the journal Current Biology. The finding shortens the timeline for how long smallpox may have afflicted humans.
- Most Americans under 40 have not been vaccinated. The last smallpox case in the United States was in 1949, and routine vaccination stopped in 1972. Some medical and military personal are still vaccinated.





Source: https://edition.cnn.com/2013/09/02/health/smallpox-fast-facts/index.html
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Market Overview – Smallpox

Current Treatment options

Treatment of smallpox patients generally involves supportive care. Vaccination can prevent or lessen the severity of disease if given within 2 to 3 days of the initial exposure. It may decrease symptoms if given within the first week of exposure.

The name of the Smallpox vaccine is **ACAM2000®**

Top Competitive landscape for TPOXX

The only other **competitor: Brincidofovir (CMX001)**is **a** product of **Chimerix (NASDAQ:CMRX)** is approximately 1 to 2 years behind in their smallpox program if their drug is also successful in completing the regulatory process.

Brincidofovir has received Fast Track designation from the U.S. Food and Drug Administration (FDA) for adenovirus, smallpox. Brincidofovir has also received Orphan Medicinal Product Designations from the European Commission for the treatment of adenovirus, the prevention of CMV disease and for the treatment of smallpox. Both oral and intravenous formulations of brincidofovir are in development.

CHIMERIX, INC.

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https://seekingalpha.com/article/4169521-siga-technologies-buy-smallpox-treatment, http://www.chimerix.com/

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