Antiviral Drugs: Adapting Capabilities for an Effective Response to Future Epidemic Outbreaks

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# NCT USA 2021

#### **Forward Looking Statements**

The statements made in this presentation may include forward-looking statements regarding the treatment of smallpox and other orthopoxvirus infections, the development and attributes of SIGA Technologies, Inc. ("SIGA") products, and the future operations, opportunities or financial performance of SIGA. Although we believe that the expectations contained in this presentation are reasonable, these forward-looking statements are only estimations based upon the information available to SIGA as of the date of this presentation. Except as required by law, we expressly disclaim any responsibility to publicly update or revise our forward-looking statements, whether as a result of new information, future events or otherwise. Thus, the forward-looking statements herein involve known and unknown risks and uncertainties and other important factors such that actual future operations, opportunities or financial performance may differ materially from these forward-looking statements.

Undue reliance should not be placed on forward looking statements, which speak only as of the date hereof. All forward-looking statements contained herein are qualified in their entirety by the foregoing cautionary statements.

For a more detailed discussion of our risks, see the Risk Factors section in SIGA's Annual Report on Form 10-K for the fiscal year ended December 31, 2020 filed with the SEC and our other filings with the SEC, including our most recent Quarterly Report, all of which are available on our website, <u>www.siga.com</u>.



#### COVID-19 has Shown the Impact of a Pandemic and Magnitude of Required Response

#### Trillions in Economic Impact; >4,260,000 Fatalities Worldwide; Over \$100B in the U.S. alone for supplemental funding for Medical Countermeasures

\$62 billion for ASPR generally to prevent, prepare for, and respond to COVID-19, domestically or internationally, including the development of necessary countermeasures and vaccines

\$19 billion for the Strategic National Stockpile for critical medical supplies, personal protective equipment, and life-saving medicine

\$10.5 billion for BARDA to advance construction, manufacturing, and purchase of vaccines and therapeutics

\$522 million for FDA review activities related to COVID-19 medical countermeasures

\$2.4 billion for NIH to expand on prior research plans, including developing an improved understanding of the prevalence of COVID19, study the long term impacts of COVID19, and support clinical trials

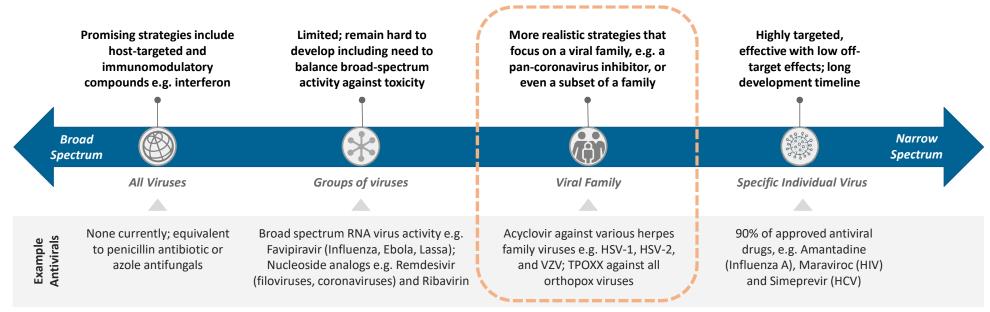
Totals don't include the over \$190 billion in other public health costs to the federal government, including direct reimbursements to hospitals and health systems, and funding for state and local response efforts



#### Effective Response Requires Development and Stockpiling of Broad-Spectrum Antivirals with Diverse Mechanisms of Action Readily Deployable for Future Epidemics

# "The scientific community really should have developed universal antivirals against SARS. Then we would have had something in the stockpile for the emergence of COVID"

Robert Webster, emeritus member of St Jude Children's Research Hospital in Memphis, Tennessee

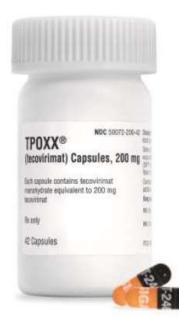


Source: The race for antiviral drugs to beat COVID — and the next pandemic. https://www.nature.com/articles/d41586-021-00958-4

#### Case Study: Smallpox Antiviral with Broad Orthopox Activity

#### Oral TPOXX<sup>®</sup> (Tecovirimat/ST-246)<sup>1,2</sup>

- FDA-approved (July 2018) novel small-molecule oral drug indicated for treatment of human smallpox disease in adults and pediatric patients ≥13 kg
- Although not yet approved for broader indication, exhibits antiviral activity against all orthopoxviruses tested *in vitro* (nanomolar concentrations) and in animal models
- No drug-related SAEs in clinical trials
- Adult Dosing: Oral capsule (200 mg/capsule)/600 mg twice a day for 14 days
- 84-months stability demonstrated for active pharmaceutical ingredient (tecovirimat monohydrate) and final drug product (TPOXX)
- More than two million courses of treatment delivered to the US Strategic National Stockpile

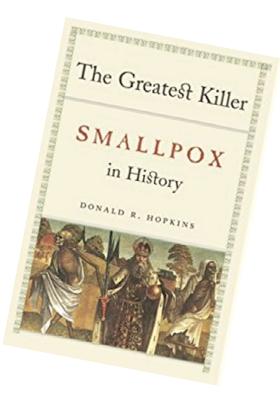


- 1. TPOXX not approved outside U.S. SIGA is seeking EMA and Health Canada approval for tecovirimat (approved by U.S. FDA as TPOXX<sup>®</sup>)
- 2. Full TPOXX prescribing information is available here: <u>https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=fce826ab-4d6a-4139-a2ee-a304a913a253</u>



#### **Smallpox: A Deadly Killer**

- Highly contagious infectious disease with a potential 30% fatality rate and was responsible for approximately 300 million deaths worldwide in the 20th century
- Symptoms included a distinctive and progressive skin rash, leaving many survivors with permanent scars over large areas of their body, especially their face. Some survivors were left blind by the disease
- Smallpox was still widespread as recently as 1966, with regular outbreaks in multiple countries across South America, Africa, and Asia
- World Health Organization ("WHO") initiative to eradicate smallpox through vaccination was largely successful and, by 1980, the World Health Assembly officially declared the world free of the disease
- Smallpox remains a concern for public health authorities, as samples of the virus have been kept for research purposes and even a single confirmed case would be considered an emergency





#### Smallpox Remains a Significant Bioterrorism Threat

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North Korea is far more likely to use biological weapons than nuclear ones. The program is advanced, underestimated and highly lethal

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Andrew C. Weber, Pentagon official in charge of nuclear, chemical and biological defense programs under President Obama,

The New York Times, 2019



Explosion at Russian Lab That Houses Smallpox Sends Internet Into Panic

"Somebody would reconstruct, say, a smallpox virus and have that spread, and that would not only kill millions, it could potentially kill billions."



Bill Gates on bioterrorism, 2017, PBS

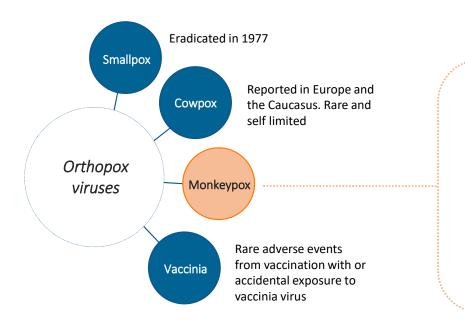
**nature** International journal of science

#### The spectre of smallpox lingers

"In 2014, the NIH discovered live stocks in a storage room on its campus in Bethesda, Maryland. If the venerable and highly regulated NIH could lose track of smallpox, other institutions could have some forgotten vials as well."

August 2018

# Viral Outbreaks are Becoming More Common, including Orthopoxviruses: The Epidemic Potential of Monkeypox is Expected to Continue to Rise



- Outbreak frequency and size in human populations have steadily increased likely due to the decline in herd immunity following cessation of smallpox vaccination
- Major health concern in DRC and other African countries such as Nigeria and the Central African Republic
- Cases of monkeypox were imported in western countries posing an increasing risk for health security; *recently cases reported in the U.K and U.S.*

TPOXX has been used as compassionate treatment for several cases of monkeypox, cowpox and vaccinia complications<sup>1</sup>. In June 2021, TPOXX was provided for the treatment of a patient with monkeypox in the U.K.

Source: https://www.pasteur.fr/en/research-journal/news/monkeypox-epidemic-potential-will-continue-increasing-diminishing-herd-immunity-against-viruses <sup>1</sup>Orbital Cowpox. Miles Kiernan and Nikolaos Koutroumanos. June 10, 2021, N Engl J Med 2021; 384:2241, DOI: 10.1056/NEJMicm2033620



Monkeypox is a Growing Public Health Threat

#### Monkeypox patient in UK hospital as officials look for others who may be infected

The person flew from Nigeria to the UK where they Foundation Trust in London for monkeypox, a disea 00:05, 14 Mar 2020 Monkeypox returns to the Central African Republic by NEWS DESK Pebruary 4, 2021

# DRC report 1,000 more monkeypox cases in 2020, Deaths double

by NEWS DESK More th O January 26, 2021 Africa No Comments monitor

More than 200 people in U.S. being monitored for possible monkeypox exposure, CDC says

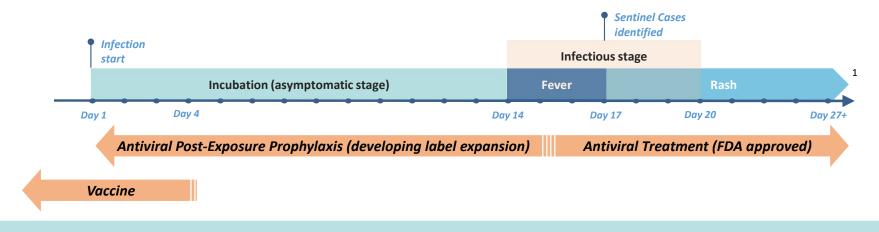
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By Helen Branswell y July 20, 2021



#### Even with Vaccination, Published Models<sup>1</sup> have Shown that Use of an Antiviral Drug During an Outbreak would Significantly Reduce Fatalities

- Mass vaccine distribution will take time and money that will not be immediately available
- COVID showed that up to 35% of the U.S. population is currently resistant to taking a vaccine
- Until an outbreak is fully contained, treatment is needed for the breakthrough cases and immunocompromised



Antiviral therapy is an essential component of biopreparedness that reduces morbidity and mortality in those diagnosed with smallpox and limits its spread in a susceptible population

<sup>1</sup>Adapted from Breman J.G. and Henderson D.A. <sup>2</sup>The role of vaccination, orthopoxvirus drug, and social cooperativity in a mathematical model of smallpox control. Harvey Ruben. Biosecurity and Bioterrorism: Biodefense Strategy, Practice and Science (2013) 11(1)



#### Joint Effort across Several U.S. Government Agencies Supported Development of TPOXX®

- NIH first supported SIGA's development of TPOXX in 2006
- SIGA as awarded an advanced development and procurement contract from BARDA for over \$500M in 2011
- SIGA received FDA approval for Oral TPOXX in 2018
- BARDA awarded a second procurement contract in 2019, which also included funds for the development of IV and Pediatric formulations of TPOXX
- Funded by the DOD/JPEO since 2019 to develop a Post Exposure Prophylaxis indication of TPOXX
- In 2020, SIGA shipped oral TPOXX to the SNS to commence replacement of expiring product that was first delivered in 2013



TPOXX is under Regulatory Review in the EU and Canada for a Broader Label Indication including Monkeypox, Cowpox, and Vaccinia Complications in addition to Smallpox



- Current Indication: smallpox treatment only
- Planned Label Expansion Strategy
  - Post-Exposure Prophylaxis
  - Other orthopoxviruses, such as Monkeypox



- Proposed Indication: all human pathogenic Orthopoxviruses (smallpox, monkeypox, cowpox, vaccinia)
- MAA Submitted July 2020
- MAA Fully validated October 2021
- Approval expected 4Q21 or 1Q22



- Proposed Indication: all human pathogenic orthopoxviruses (smallpox, monkeypox, cowpox, vaccinia)
- NDS Submission: December 2020
- NDS Fully accepted February 2021
- Approval expected 4Q21 or 1Q22



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