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- Hello and welcome to BARDA Industry Day. My name is Karen Martins and I'm Acting Branch Chief for Antivirals and Antitoxins in the CBRN division. I'm excited to be here with you today to share some of the incredible accomplishments from our team in FY 21 and to discuss goals and strategies for FY 22 and beyond.

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As an authority under ASPR, BARDA lives the mission of saving lives and protecting Americans from health security threats. Specifically in AVAT, we focus on biological threats that have been identified as posing a material threat to the American people.

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We employ the BARDA Model to develop medical countermeasures using flexible, nimble authorities, multi-year funding and cutting edge subject matter expertise to facilitate partnerships and promote innovation. While this has been seen most publicly in the USG COVID 19 response, this operational approach pervades all activities within BARDA, including AVAT.

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Within AVAT, our focus is on protecting the population by developing and maintaining safe and effective therapeutics for anthrax, botulism, smallpox, and filoviruses. For FY22, we are focused both on maintaining and enhancing our existing portfolio, as well as expanding our portfolio through market research and engagement with potential partners in the research and development space.

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New products that compliment our existing portfolio are of course, always of interest and FY22 will have a specific focus on antivirals with efficacy against the filoviruses and with the potential for broad-acting activity against multiple species within relevant to narrow, or families as will be discussed further later.

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But before diving into the future, I'd like to take a moment to reflect on a fantastic year for AVAT. Under the leadership of David Boucher, AVAT supported the 56th and 57th product licensures for BARDA with the licensure of two antibody products with efficacy against Ebola virus, a task which seemed almost unachievable a decade ago.

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In October of 2020, Inmazeb, a three antibody cocktail developed by Regeneron was the first Ebola virus therapeutic to achieve licensure. Only two months later, a second monoclonal antibody product, Ebanga, developed by NIAID and Ridgeback followed suit.

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Both of these products had been on a path to licensure through FDA's Animal Rule. However, nature and a tremendously hardworking group of individuals from NIAID, the INRB and The Democratic Republic of Congo, the US interagency and the international community came together to conduct a randomized clinical trial in DRC in 2018 and 2019. The results of that trial showed that mAb114 and EB3 as they were known at the time were superior to the control arm and those products ultimately advanced to licensure under the traditional pathway.

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BARDA worked closely with the FDA, the interagency and the product sponsors to support licensure in an incredibly rapid timeframe. Our regulatory and quality affairs team and manufacturing subject matter experts worked tirelessly with the product sponsors to respond to FDA information requests, turning around comments within 24 hours to enable the sponsors to meet critical deadlines.

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The licensure of these products is an outstanding example of the type of public private partnerships that make BARDA so effective. In June of this year, AVAT about let a third product through to licensure this time for the smallpox indication, Tembexa, a lipid encapsulated prodrug of cidofovir was licensed for the smallpox indication through the FDA's Animal Rule. This approval means that there are now two antivirals with complimentary mechanisms of action available to respond to the smallpox threat, which substantively increases our ability to respond if needed.

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So where are we today? Presented here is an overview of the AVAT portfolio. Our focus is again on threats with the DHS issued and material threat determination, which include filoviruses, anthrax, smallpox, and botulism toxins. Within the filovirus area we have, of course, the two licensed products for Ebola, Ebanga and Inmazed and in development our antibody-based products for Marburg virus and Sudan virus, the latter of which is being evaluated in phase one clinical trials at this time.

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In the smallpox portfolio, we supported the licensed products, Tembexa and tecovirimat and we are also working with BioFactura on a preclinical antibody product. And finally, in terms of anthrax antitoxins, three antibody products are licensed, the monoclonal antibodies, Anthim and raxibacumab and Anthrasil, a polyclonal antibody product.

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In addition to hBAT the licensed polyclonal antibody product with efficacy in C. bot neurotoxins, we are working with Mapp Biopharmaceuticals to develop next gen pan-BoNT cocktail. So I'd like to take this opportunity to deep dive into the various program areas. The licensure of Ebanga and Inmazed is a significant accomplishment that I would not want to understate. In the PALM study, the product significantly reduced death from Ebola virus disease. Mortality in the control arm was approximately 50%. It was approximately 34% in the two treatment arms.

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Moreover, of the 16 patients who received one of these two therapeutics in outbreaks earlier this year, 14 have recovered. However, we do not feel that the problem of Ebola virus can be considered solved. We are very much interested in treatments that may reduce mortality even further and have demonstrated efficacy in preclinical models of severe infection.

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Also, as observed with the outbreaks in DRC and Guinea this year, persistent infection and sexual transmission from EBD survivors, even months after primary infection, is an issue that must be addressed. So interventions that address persistent infection that penetrate immune-privileged sites and that address long-term sequelae associated with infection are all of interest to AVAT. We also have a specific interest in antivirals with anticipated efficacy against multiple species or generic filovirus, or a broader efficacy against RNA viruses as a whole.

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With the exception of Ebola virus, there are no approved therapeutics for other viruses in the Filoviridae family. In FY22 BARDA will continue to work with Mapp Biopharmaceutical to advance Mapp products for MBP091 and MBP134 for the Marburg virus and Sudan virus indications respectively. Barring an unexpected and large outbreak of either virus, licensure of these products will likely be through FDA's Animal Rule. Therefore, part of that effort involves close engagement with BARDA's nonclinical group, which helps support the MCM portfolios with NHV Natural History Studies and other preclinical evaluations.

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With respect to potential new starts, we're interested in products with strong preclinical data, broad filovirus activity and/or the potential to compliment antibody-based products. While there's limited clinical data available on filoviruses other than Ebola virus, we anticipate that some of the same issues of persistent infection and long-term sequelae may be relevant for other filoviruses.

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We are therefore interested in products with the potential to address those risks. For smallpox, considering the two licensed smallpox therapeutics, BARDA's focus in FY22 will be on continuing to support and expand the utility of these products, while also advancing antibody-based product that's in development by BioFactura. Any new starts in the smallpox area of interest, would need to demonstrate significant benefit over the existing products, either in terms of efficacy, or operational parameters.

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Finally, turning to the antitoxin portfolio, as noted previously, three anthrax anti-toxin products have been licensed and are available as needed. We're also working with Mapp Biopharmaceuticals on the next gen anti-BoNT neurotoxin product to supplement and license that.

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We're always open to novel approaches to address the challenge of anthrax and BoNT neurotoxins, or products that may improve our readiness to respond to a large-scale aerosol anthrax exposure. So to wrap up, AVAT has supported licensure, three medical countermeasures in the last fiscal year and four AVAT threat areas, as defined by DHS MTDs, currently have approved products available for use.

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While we hope to never have to use the products that are developed in AVAT, in FY21 alone, AVAT supported the response to the Ebola virus outbreaks, including the ongoing outbreak in DRC, as well as a Marburg virus outbreak in Guinea. In addition, we helped ensure that TPOXX was deployed to treat a patient diagnosed with monkeypox. In the years to come we will aim to improve access to medical countermeasures with emphasis on manufacturing, formulation and procurement.

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New starts will be evaluated by their potential for improved efficacy or operational logistics. We're also interested in antivirals with efficacy, not only against filovirus and orthopoxviruses, but with the potential for broad antiviral activity. This category would include products, targeting conserved viral proteins, or products targeting host proteins that are critical for viral pathogenesis.

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We would specifically be looking for a well-described mechanism of action that has a likelihood of efficacy against multiple virus species within a family and those products that have the potential to be orally available would be a specific interest as well.

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I'd encourage developers with products that fit that description to look at the recent revisions to our BAA area of interest number two. With that, I'd like to acknowledge our AVAT team, specifically David Boucher, who has served as branch chief until recently, stepping back to dedicate his time to the COVID-19 response efforts.

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We have an outstanding team of project officers who are excited to work with all of you in the future. I'd also like to think BARDA's Contracting Office, Core Services and perhaps most importantly, our industry partners who make it possible to advance these products for the good of the American people in the world. Here are some links to some of the websites, social media, for more information about AVAT and about CBRN in general. And of course, follow us on social media for the latest information. Thank you so much.