ADVAXIA BIOLOGICS

World Vaccine Congress Europe 2022

Viral Vector Vaccines: Adenoviruses

Stefania Di Marco

Oct 13, 2022

Advaxia (formerly Advent)

- Established in 2010 and located in the main IRBM site of Pomezia-Rome

- GMP facility, accredited by AIFA since 2012
- Dedicated to R&D and GMP production of biological investigational medicinal products: **Investigational adenovirus vaccines for infectious diseases and gene therapy applications**

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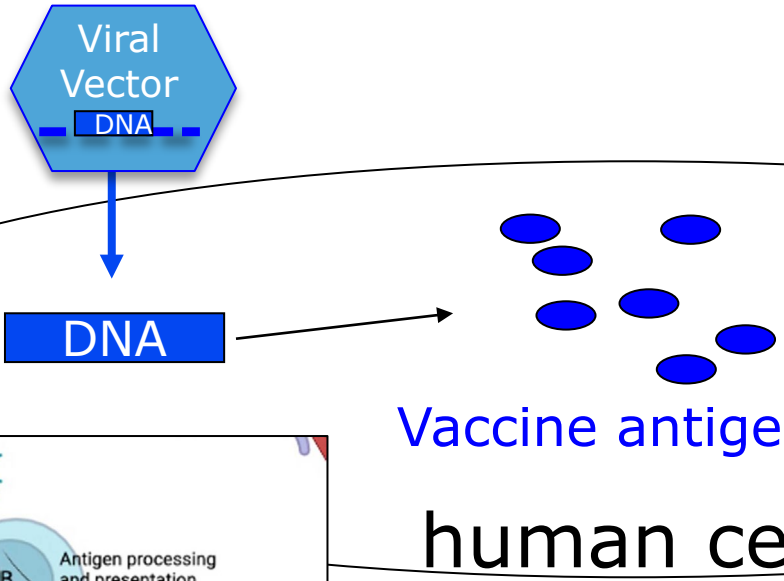
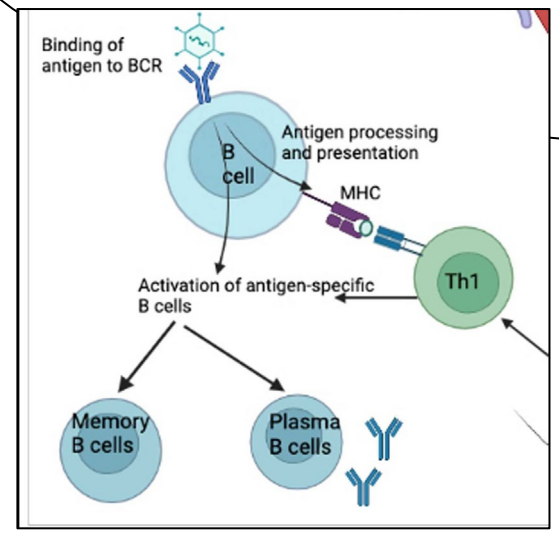
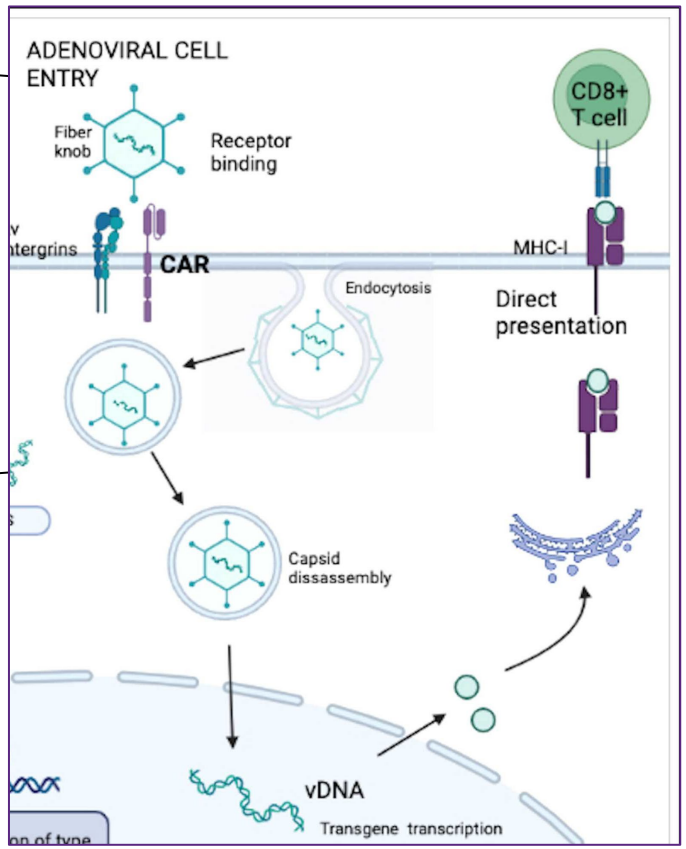
To efficiently prevent viral infection it is necessary to activate the two arms of the adaptive immune system, T cells and Antibodies: Viral Vector Vaccines induce both







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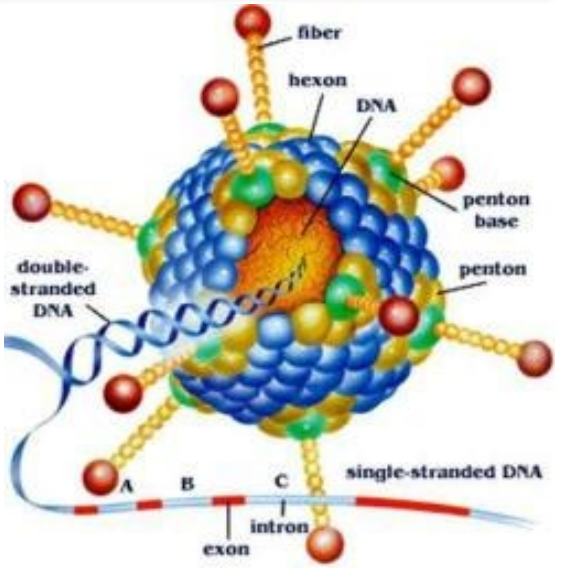
Viral Vector Vaccines: Adenoviruses

Pros

- Infect dividing and non-dividing cells
- Double strand 36 Kb DNA, easy to manipulate
- It does not integrate
- Broad tissue tropism
- Well known biology

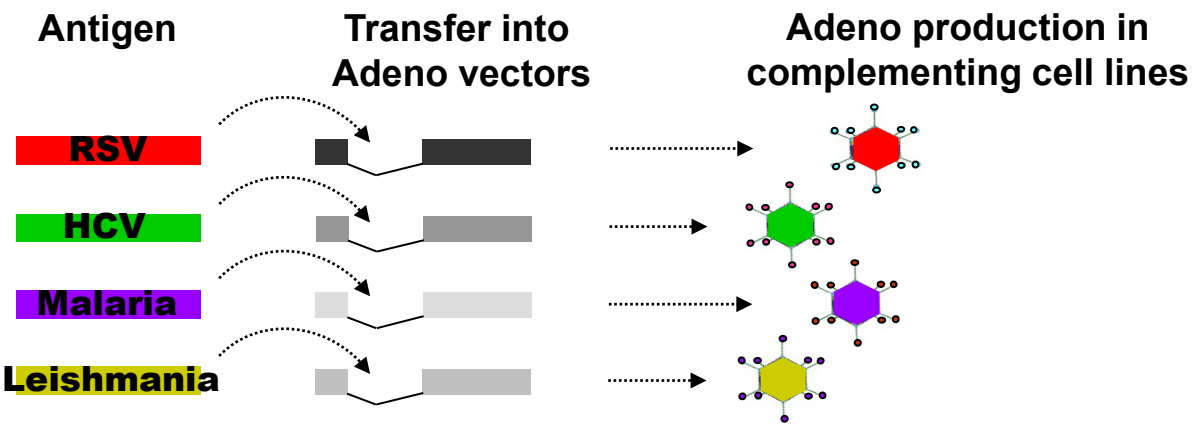


Cons

- Pre-existing immunity against the Ad vector reduces immunogenicity and thus protective effects of these vaccine vectors (relevant with Ad5-based vector vaccines given their high seroprevalence in humans)

Adenovirus Platform: To circumvent the issue of anti-vector immunity, less prevalent Ads, non-human Ads, have been developed

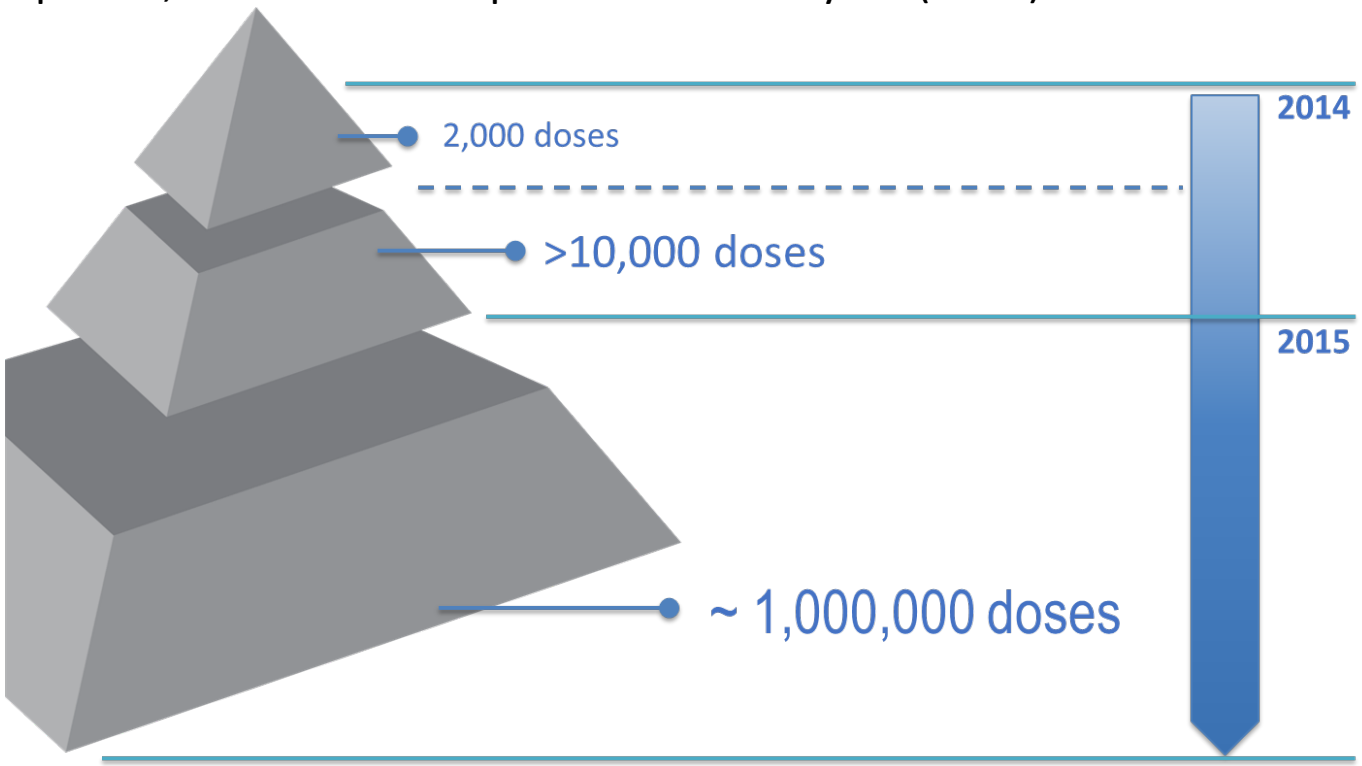
- Replication deficient by E1 and/or E3 gene deletion
- Produced in E1 complementing cell lines (HEK-293 derived)
- Cloning capacity > 9 Kb. Maximum antigen length tested: 2,200 amino acids
- Identical strategy for development & manufacturing of different vaccines
- Ease of production & scalable



- *Chimpanzee adenovirus- and MVA-vectored respiratory syncytial virus vaccine is safe and immunogenic in adults. Sci Transl. Med. 7(300), 2015*
- *Chronic Hepatitis C Virus infection subverts vaccine induced T cell immunity in humans. Hepatology, 63, 1455, 2016*
- *Human vaccination against RH5 induces neutralizing antimalarial antibodies that inhibit RH5 invasion complex interactions. Journal of Clinical Investigation Insight, 2(21), 2017*
- *A third generation vaccine for human visceral leishmaniasis and post kala azar dermal leishmaniasis: First-in-human trial of ChAd63-KH. PLoS neglected tropical diseases 11 (5), 2017*

2015. Ebola Epidemic

- Production scaling-up during Ebola emergency for ChAd3 Ebola vaccine development, 1 million doses produced in one year (2015)



- Clinical trials performed with ChAd3 vaccine encoding the glycoprotein of the Zaire strain of Ebola. The vaccine is safe, well tolerated and induces antibodies and T cells. *N. Engl. J. Med. Jan 28,* 2015; *N. Engl. J. Med. 374, 1635,* 2016

2020. SARS-CoV-2 Pandemic

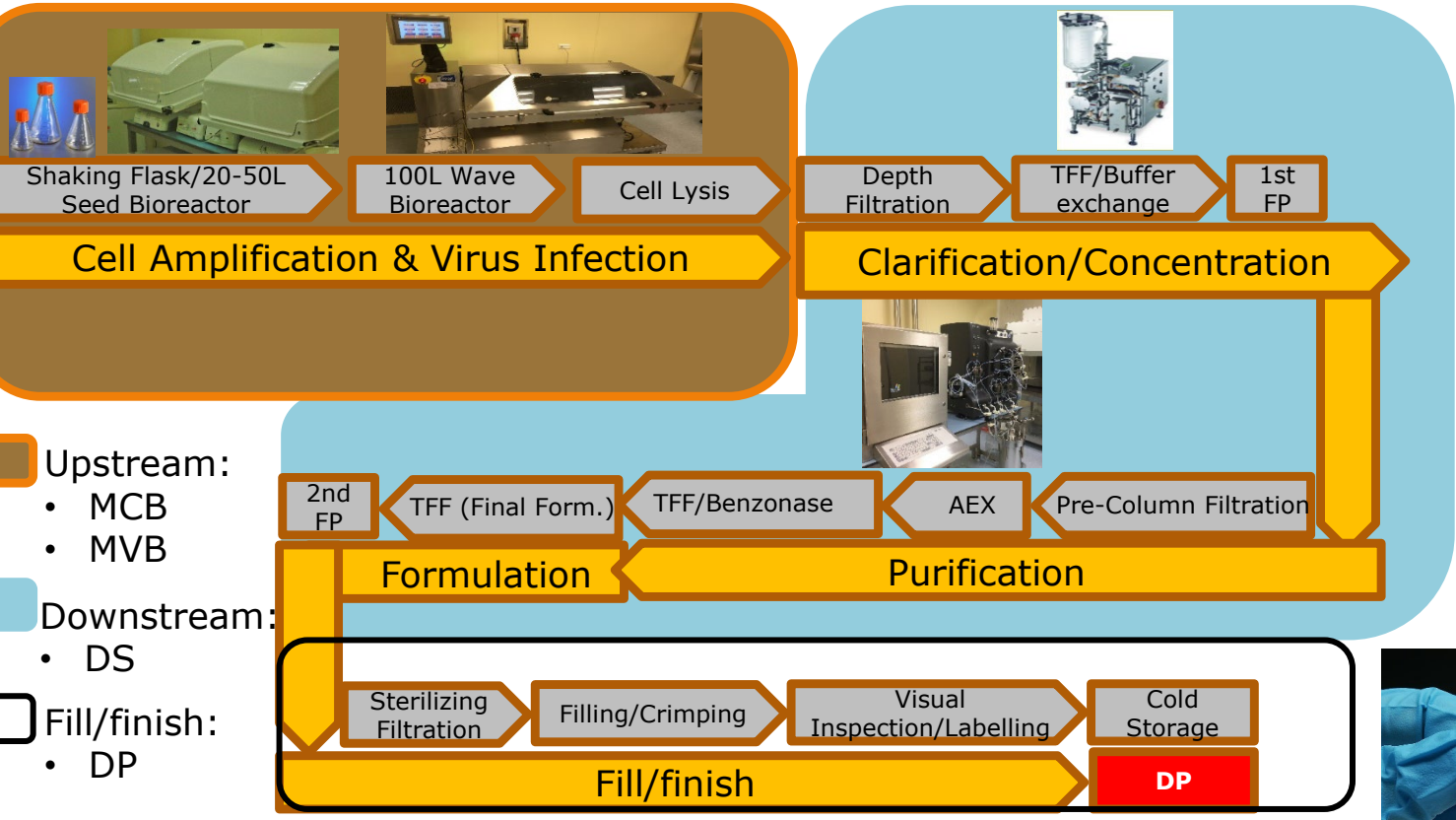
Exploiting the ChAdOx1 vaccine platform

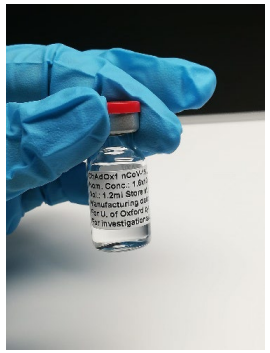
Prior knowledge of

Manufacturing process	➢ **Efficient and scalable**
Safety and reactogenicity	➢ **Good safety profile in adults, children, infants, elderly and HIV+ individuals**
Immunogenicity	➢ **Both humoral and cellular immunogenicity**

- ✓ In the case of SARS-CoV, only antibodies directed to the spike protein can neutralize the virus and prevent infection. *Buchholz et al. PNAS, 2004*
- ✓ A single dose of ChAdOx1 MERS, a chimpanzee adenovirus vectored vaccine that encodes the spike protein of Middle East respiratory syndrome coronavirus (MERS-CoV), protected non-human primates against MERS-CoV induced disease. *van Doremalen N, Haddock E, Feldmann F, et al. Sci Adv 2020*
- ✓ Data from a phase 1 clinical trial showed that ChAdOx1 MERS was safe, well tolerated and the highest dose elicited both humoral and cellular responses against MERS-CoV in all vaccinees within 1 month of vaccination. *Folegatti PM, Bittaye M, Flaxman A, et al. Lancet Infect Dis 2020*

Manufacturing Process applied to ChAdOx1 nCoV-19 vaccine





ChAdOx1 nCoV-19
Generation of the Drug Substance

Packaging cell line amplification in bioreactor

Cell infection with the viral bank & harvest

Cell lysis by detergent

Downstream process based on TFF & AEX chromatography

Formulation, 0.22 um filtration & storage at <-60°C

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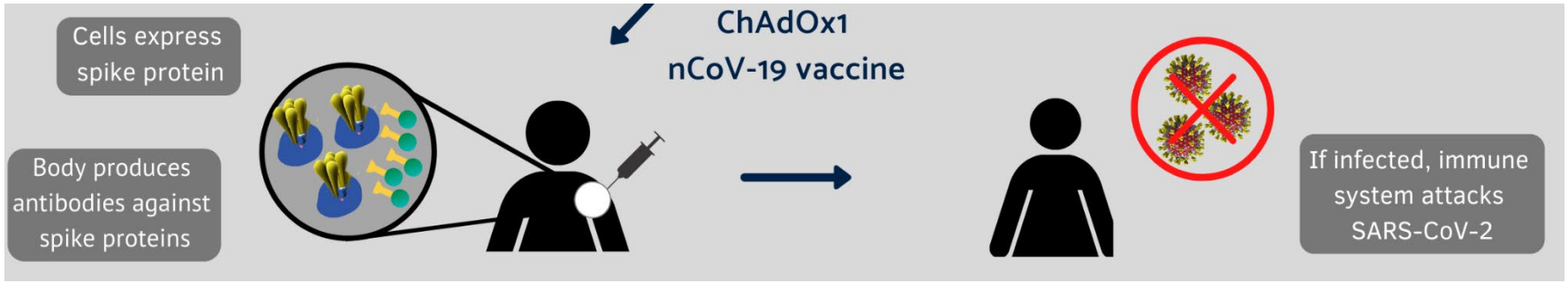
Covid-19 Emergency Needs: the ChAdOx1 nCoV-19 vaccine



- COVID-19: An Adaptive Phase I/II Randomized Placebo-controlled Trial to Determine Safety, Immunogenicity and Efficacy of Non-replicating ChAdOx1 SARS CoV-2 Vaccine in South African Adults Living Without HIV; and Safety and Immunogenicity in Adults Living With HIV. 2000 participants, **PACTR20200692216513, South Africa**

- A phase Ib/II single-blinded, randomised, controlled study to determine safety, immunogenicity and efficacy of the candidate Coronavirus Disease (COVID-19) vaccine ChAdOx1 nCoV-19 in adults in Kenya, (COV004). **PACTR202005681895696, Kenya**

- COV002: A phase 2/3 study to determine the efficacy, safety and immunogenicity of the candidate Coronavirus Disease (COVID-19) vaccine ChAdOx1 nCoV-19. 10560 participants, **EudraCT number 2020-001228-32, UK**

- COV003: A phase III randomized controlled trial to determine safety, efficacy, and immunogenicity of the non-replicating ChAdOx1 nCoV-19 vaccine, 5000 participants, **ISRCTN89951424, Brazil**

Lancet 2020, 396: 467–78; Lancet 2021, 396:1979-1993; Lancet 2021, 397:99-111

Vaccine Authorizations: Dec 2020 (UK); Jan 2021 (EMA); Feb 2021 (WHO)

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Thank you!

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<Supplemental Slides>

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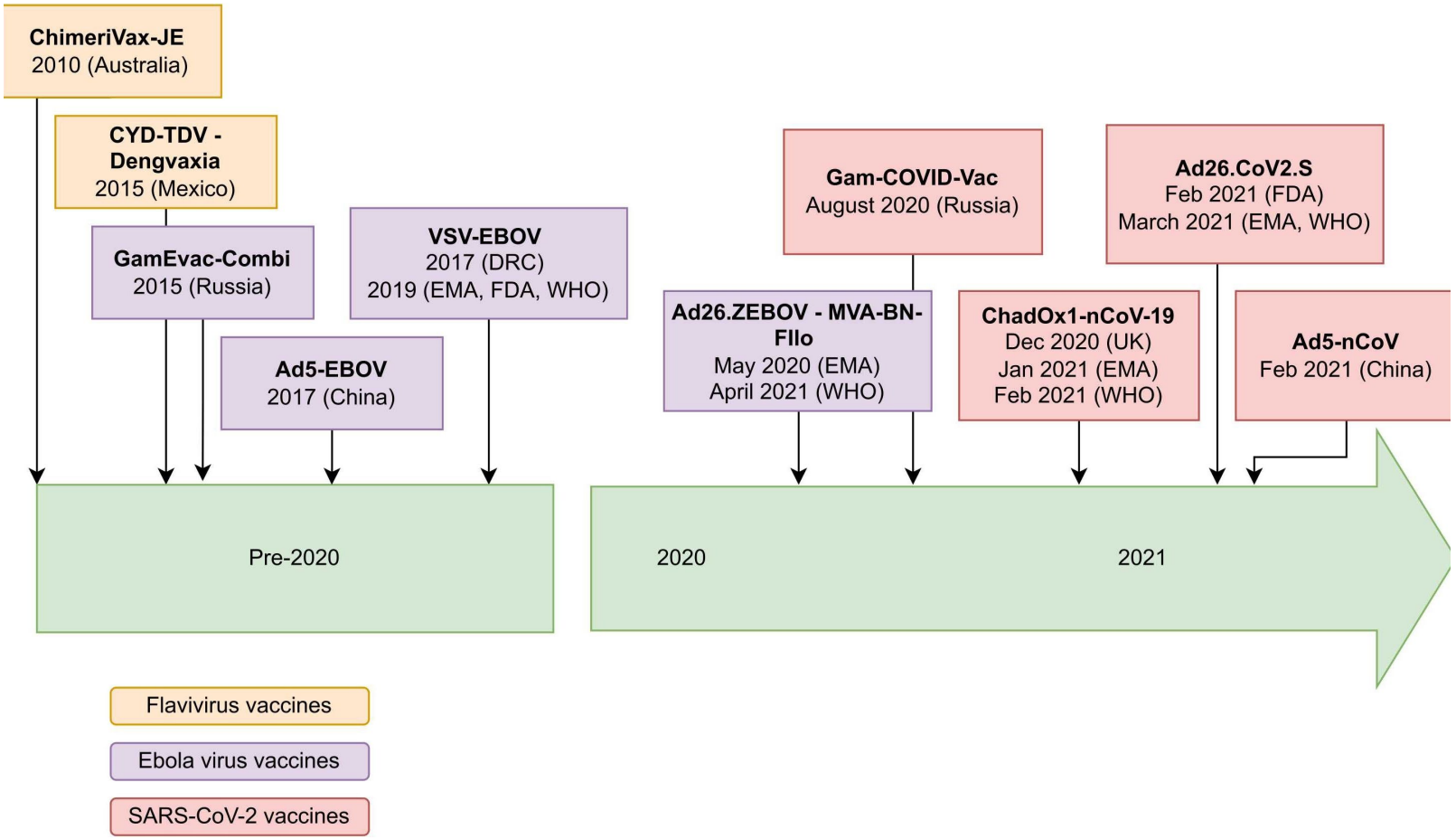
Viral vector vaccines approved for use in humans



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