



Program Pack

HIV (mRNA-1644/1574)

# Human immunodeficiency virus (HIV) overview

**HIV is the virus responsible for acquired immunodeficiency syndrome (AIDS), a lifelong, progressive illness with no effective cure**

## Disease burden

- 38 million worldwide are currently living with HIV<sup>2</sup>; 1.2 million in the U.S.<sup>3</sup>
- Approximately 1.5 million new infections are acquired worldwide each year, and ~680,000 people die<sup>2</sup>
- Primary routes of transmission are sexual intercourse and IV drug use, putting young adults at highest risk of infection<sup>3</sup>
- From 2010 to 2015, a total of \$562.6 billion was spent globally on care, treatment, and prevention of HIV<sup>4</sup>, representing significant economic burden

## Target population

- Young adults with focus on high-risk populations

## Unmet need

- No approved HIV vaccine and no effective cure

### HIV & AIDS disease progression<sup>1,2</sup>

#### Acute HIV infection

*Highly contagious*

- Fever, chills
- Rash
- Sore throat
- Fatigue, muscle aches
- Mouth ulcers

#### Chronic HIV infection

*Clinical latent but still able to infect others*

- Frequently asymptomatic

#### AIDS

*CD4 count <200 cells/mm*

- Rapid weight loss
- Fevers, night sweats
- Extreme fatigue
- Opportunistic infections (e.g. candidiasis, Kaposi's sarcoma)
- Death

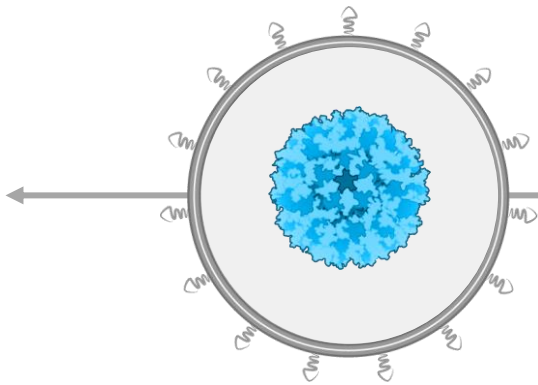
<sup>1</sup>HIV. Centers for Disease Control and Prevention. <https://www.cdc.gov/hiv/basics/whatishiv.html>. Accessed 17Dec2020. <sup>2</sup>HIV Global Statistics. <https://www.hiv.gov/hiv-basics/overview/data-and-trends/global-statistics>. Accessed 16Dec2020. <sup>3</sup>Centers for Disease Control and Prevention. HIV Surveillance Report, 2018 (Updated); vol.31. <http://www.cdc.gov/hiv/library/reports/hiv-surveillance.html>. Published May 2020. Accessed 18Dec2020. <sup>4</sup>Global Burden of Disease Health Financing Collaborator Network. Spending on health and HIV/AIDS: domestic spending and development assistance in 188 countries, 1995–2015. *Lancet* 2018;391:1799–829.

# HIV: Two complementary approaches in the clinic that tackle key challenges for making HIV vaccines

1

## mRNA-1644

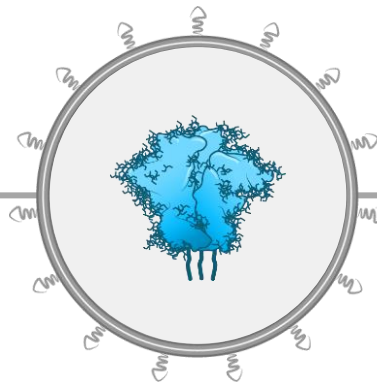
Target B cells that produce broadly neutralizing antibodies



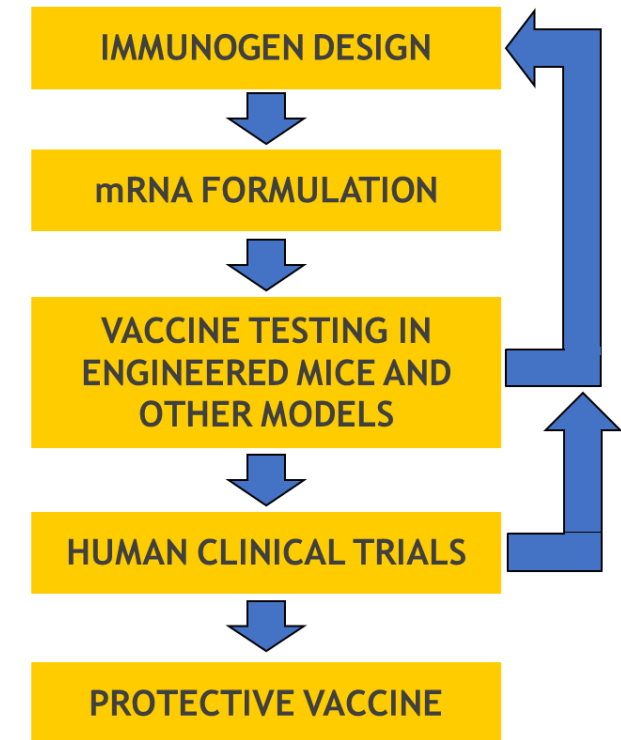
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## mRNA-1574

Native like HIV trimers



## Iterative Vaccine Design/Test Cycle

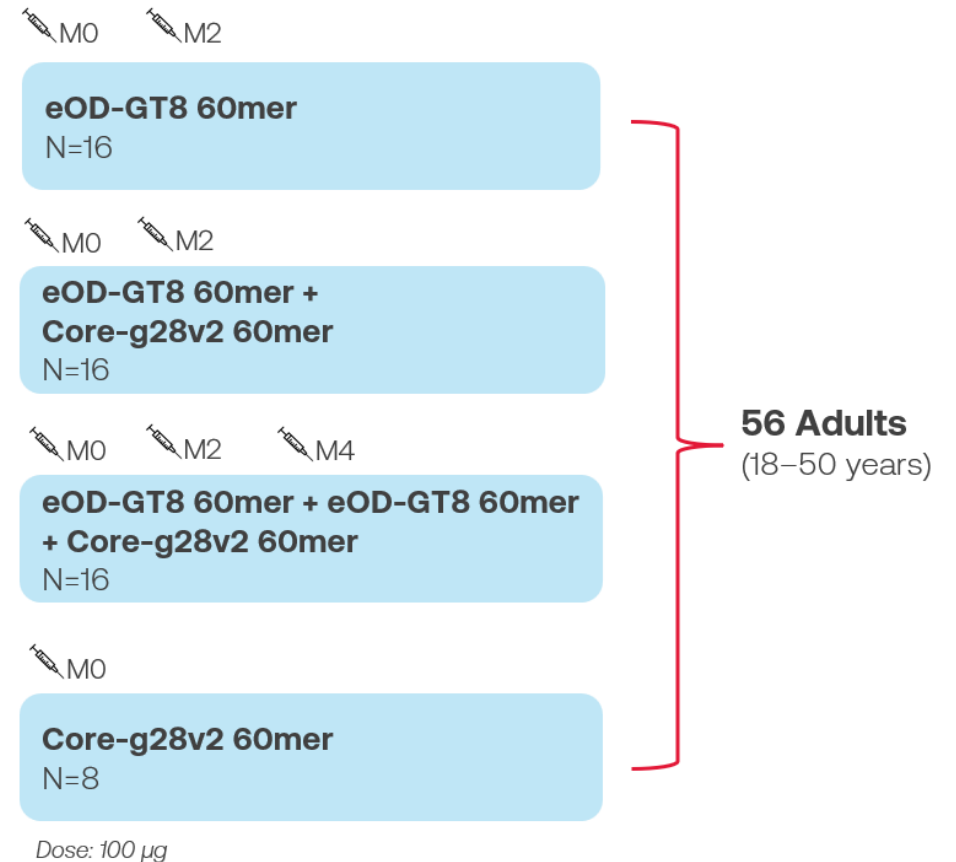


# HIV Vaccine (mRNA-1644): Germline targeting approach



- **Phase 1, randomized, open-label study** to evaluate the safety and immunogenicity of eOD-GT8 60mer mRNA Vaccine and Core-g28v2 60mer mRNA Vaccine in HIV-1 uninfected adults
- **The induction of bnAbs is widely considered to be a goal** of HIV vaccination
- **Testing hypothesis that sequential administration of priming and boosting HIV immunogens delivered mRNA can induce specific classes of B-cell responses** and guide their early maturation toward broadly neutralizing antibody (bnAb) development
- Immunogens being tested were developed by scientific teams at IAVI and Scripps Research
- mRNA-1644 phase 1 trial is ongoing

## Phase 1 Trial Design



# HIV vaccine (mRNA-1574): Trimer approach



## mRNA-1574

- **Open-label, multicenter, randomized Phase 1 study** to evaluate the safety and immunogenicity of experimental HIV trimer mRNA vaccines (BG505 MD39.3, BG505 MD39.3 gp151, and BG505 MD39.3 gp151 CD4KO)
- **Primary hypothesis is that the soluble and membrane-bound HIV envelope trimer mRNA vaccines will be safe and well-tolerated** by HIV-uninfected individuals and will elicit autologous neutralizing antibodies
- Envelope trimers being evaluated in this study were developed by William Schief, Ph.D. (professor at Scripps Research and director at IAVI) and colleagues
- mRNA-1574 phase 1 trial is ongoing

### Phase 1 Trial Design

#### Part A



##### **BG505 MD39.3**

Dose: 100 µg, N=18



##### **BG505 MD39.3 gp151**

Dose: 100 µg, N=16



##### **BG505 MD39.3 gp151 CD4KO**

Dose: 100 µg, N=16

#### Part B



##### **BG505 MD39.3**

Dose: 250 µg, N=18



##### **BG505 MD39.3 gp151**

Dose: 250 µg, N=16



##### **BG505 MD39.3 gp151 CD4KO**

Dose: 250 µg, N=16

# Forward-looking statements

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including regarding: Moderna's clinical trials; hypotheses being tested in the trials of mRNA-1644 and mRNA-1574; and expected market opportunity. In some cases, forward-looking statements can be identified by terminology such as “may,” “should,” “expects,” “intends,” “plans,” “aims,” “anticipates,” “believes,” “estimates,” “predicts,” “potential,” “continue,” or the negative of these terms or other comparable terminology, although not all forward-looking statements contain these words. The forward-looking statements in this presentation are neither promises nor guarantees, and you should not place undue reliance on these forward-looking statements because they involve known and unknown risks, uncertainties and other factors, many of which are beyond Moderna's control and which could cause actual results to differ materially from those expressed or implied by these forward-looking statements. These risks, uncertainties and other factors include those described in Moderna's most recent Annual Report on Form 10-K filed with the U.S. Securities and Exchange Commission (SEC) and in subsequent filings made by Moderna with SEC, which are available on the SEC's website at [www.sec.gov](http://www.sec.gov). Except as required by law, Moderna disclaims any intention or responsibility for updating or revising any forward-looking statements in this presentation in the event of new information, future developments or otherwise. These forward-looking statements are based on Moderna's current expectations and speak only as of the date referenced on the first page.