Prospects for a SARS-CoV-2 Vaccine

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July 1, 2020

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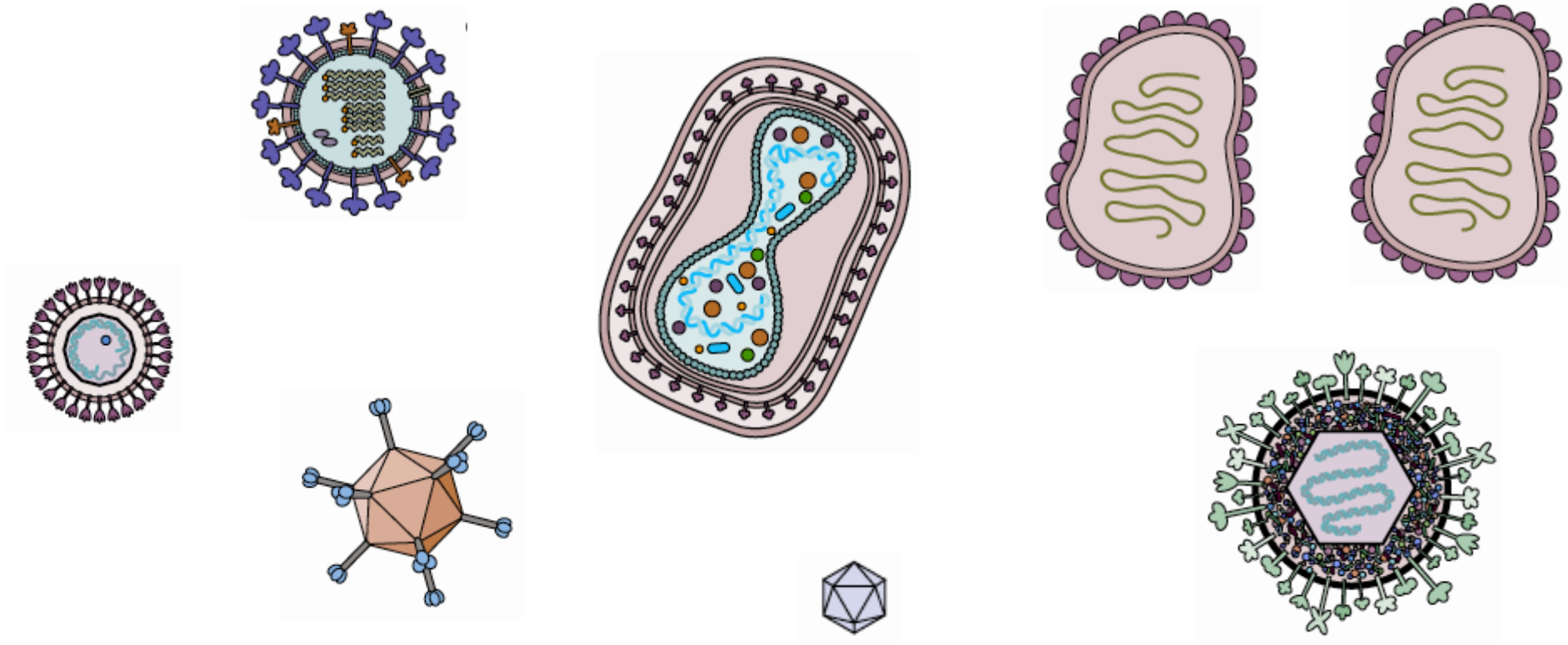
Viruses for which we have vaccines



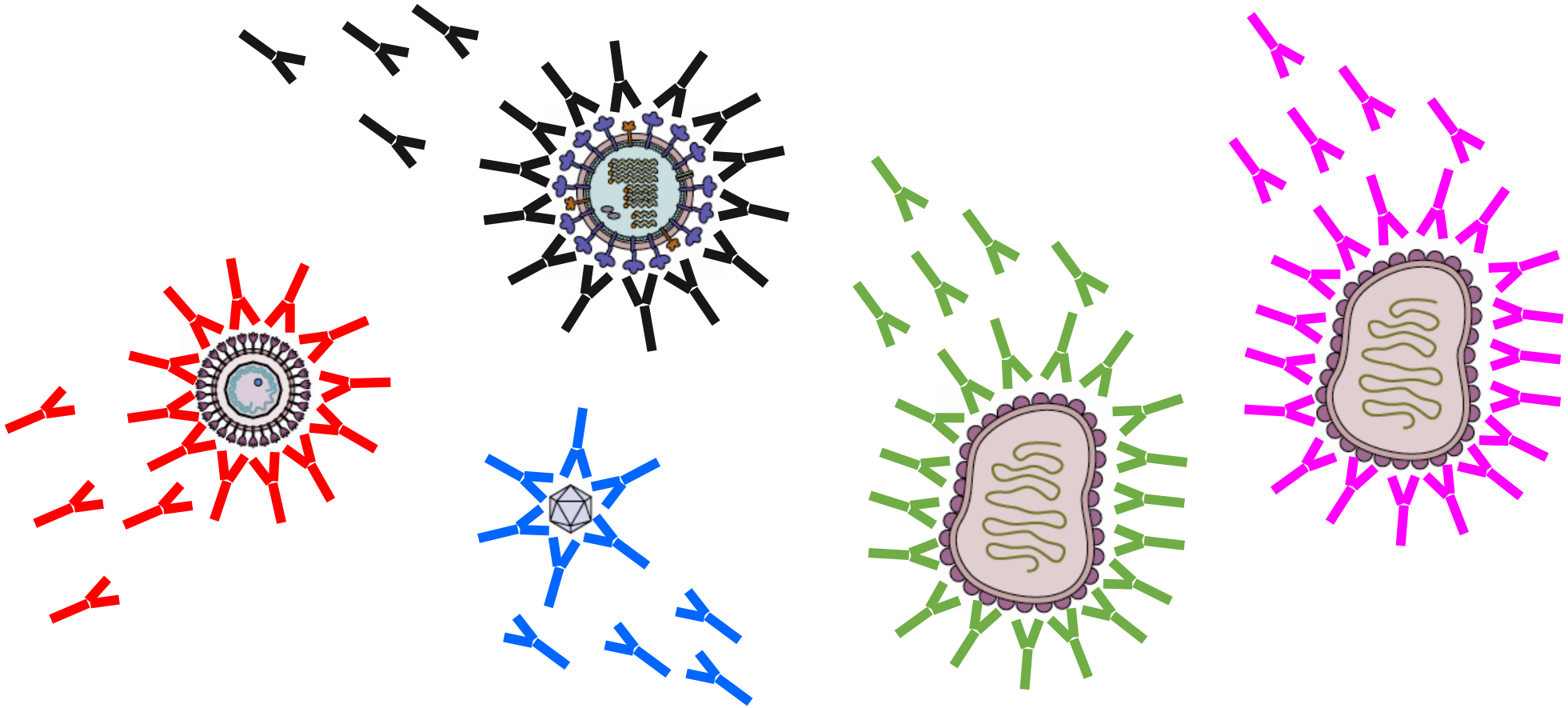
Vaccines stimulate 3 major arms of immunity

<u>Antibody</u>
Blocks initial infection

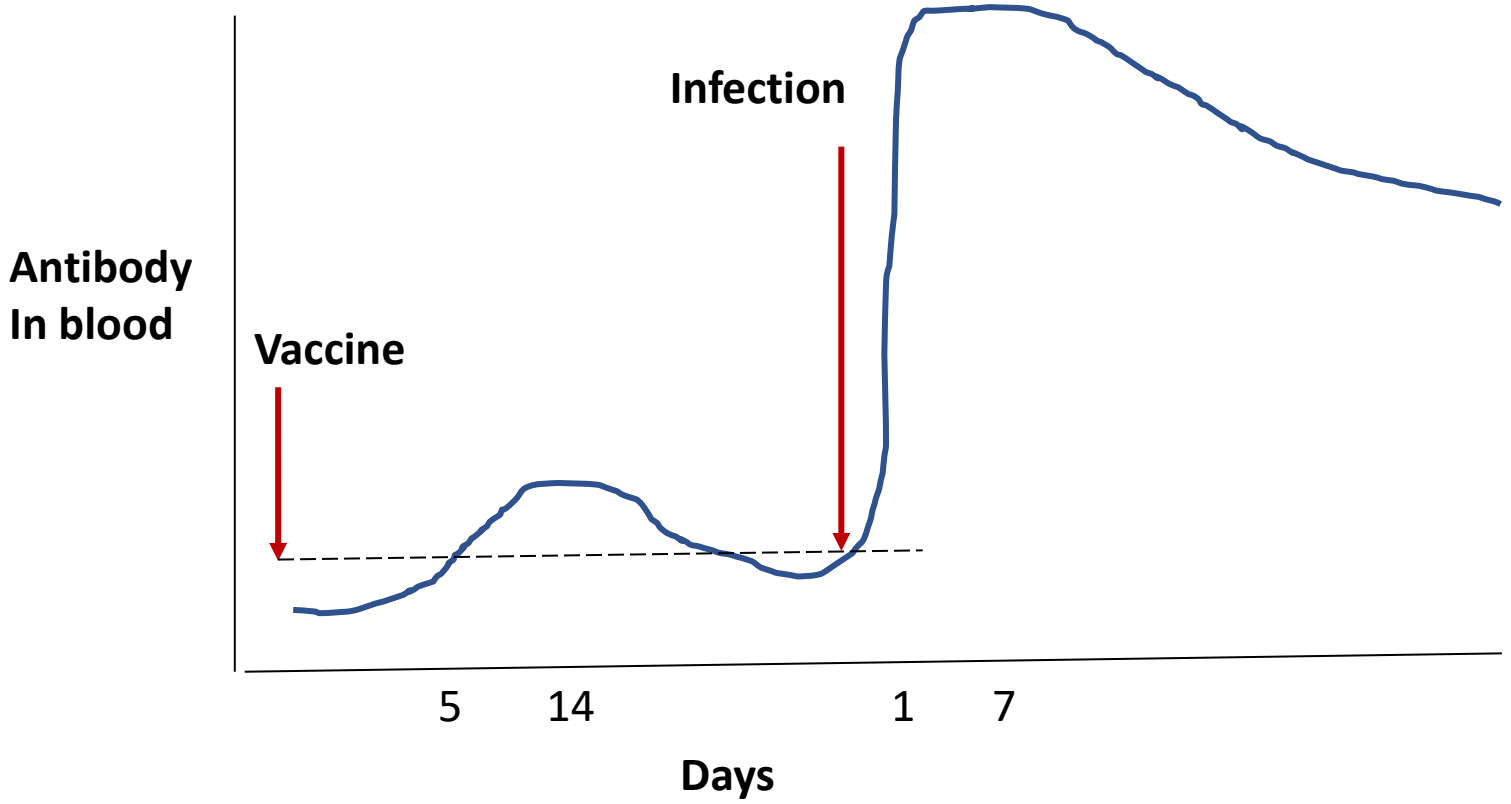
<u>Innate immunity</u>
Hypes up immune system

<u>T cells</u>
Kill cells infected by virus that gets past antibody

Antibodies that block (neutralize the virus) are the 1st line of defense

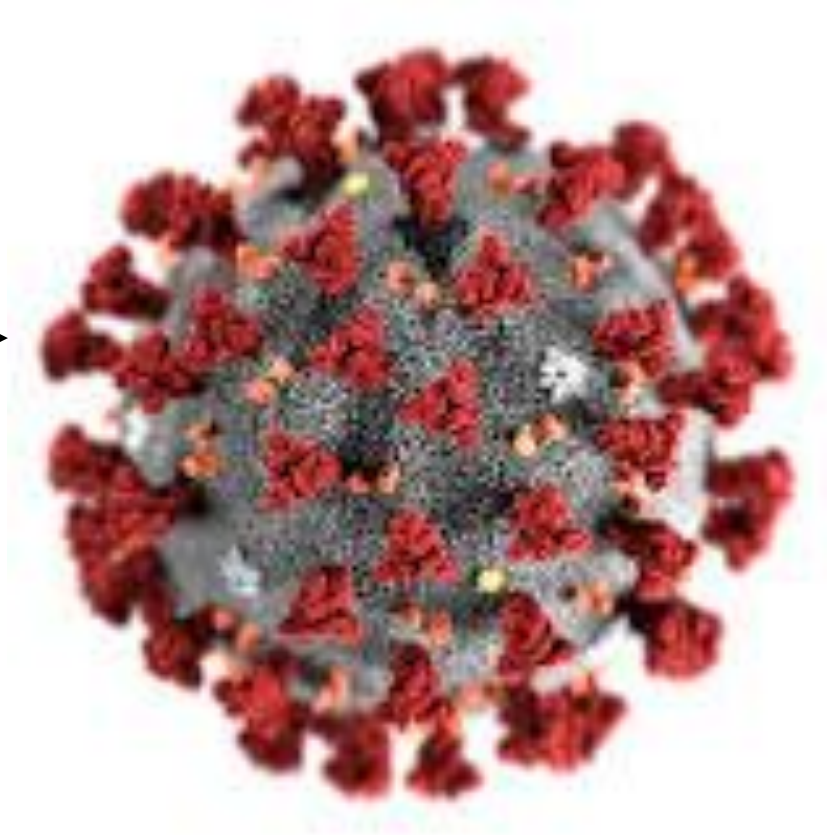


Vaccines establish memory cells for rapid and high antibody production



Major target for SARS-CoV-2 antibody

S, spike protein →

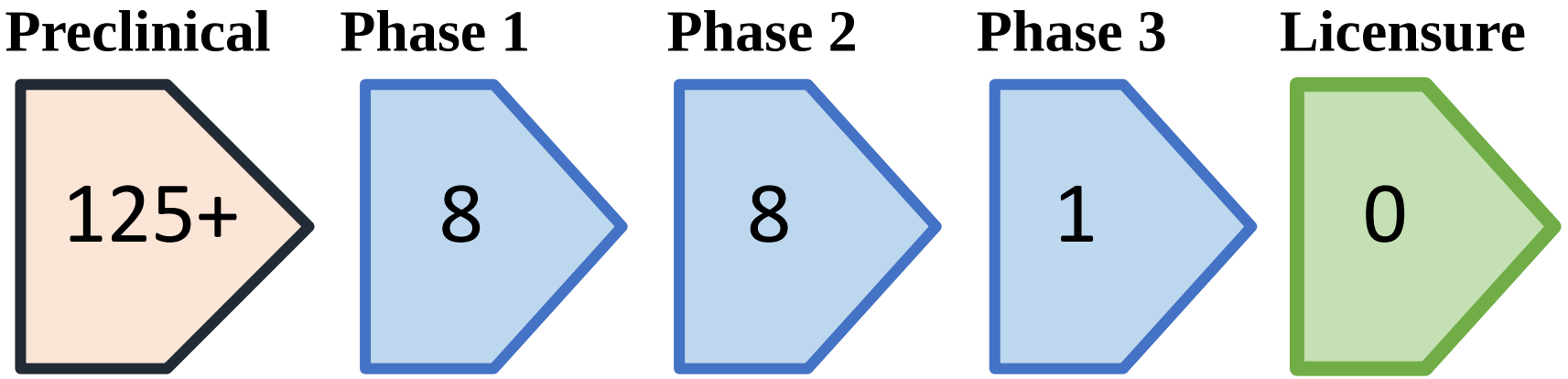


- Demonstrated that S protein can raise neutralizing antibody
- Neutralizing antibody correlates with protection of non-human primates

Risks for a SARS-CoV-2 vaccine

- **Most candidate vaccines use new recombinant DNA approaches and structure-based designs**
  - Fast – days not months to make
  - But limited experience
    - Require adjuvants, specialized delivery systems
    - Likely to require 2 doses (prime and boost)
- **Vaccinating for a new virus**
  - Risk of immune enhancement (seen for a SARS S subunit vaccine)
  - Unknown durability of antibody
  - Unknown potential to escape vaccine-elicited antibody

Current Pipeline for SARS CoV-2 vaccines



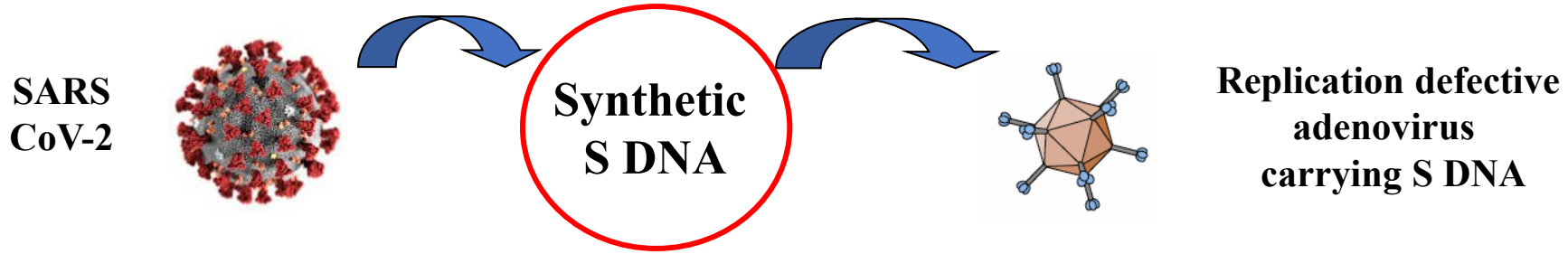
New York Times, June 16, 2020

Most advanced in human trials

- **Vaccines based on recombinant DNA approaches**
  - 3 - adenovirus (Ad) vectored vaccines
  - 2 - RNA vaccines
  - 1 - DNA vaccine
- **Protein-based vaccines**
  - 1 - Subunit vaccine
  - 2 - Whole inactivated vaccines

Data as of 6/30/20

Ad vectored vaccines

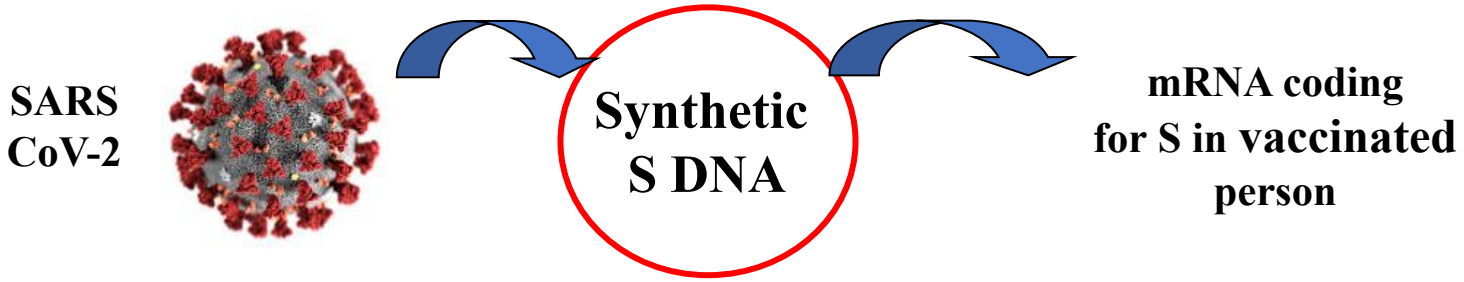


- **Oxford / AstraZeneca – England/Sweden**
  - ChAdOx1 - using a chimp Ad vector to avoid pre-existing immunity to human Ad vectors
  - Phase 3 efficacy trial (n=6000)
- **CanSino Biologics – China/Canada**
  - Ad5 vector - using a high dose to overcome pre-existing immunity
  - Phase 1 /2 human trials
- **Harvard / J&J – US**
  - Ad26 vector - using a rare serotype to avoid pre-existing immunity

Ad vectors have good manufacturability, Ad5 has a poor safety history for HIV

Data as of 6/30/20

RNA vectored vaccines

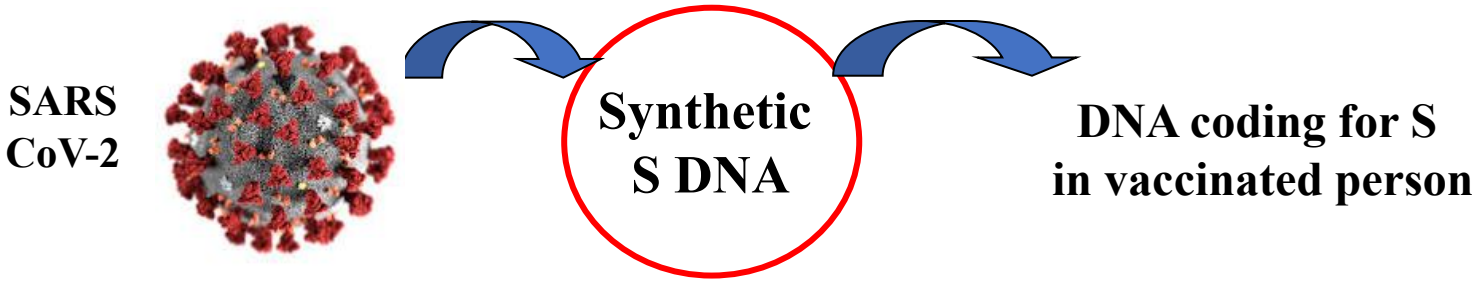


- **Moderna/NIH Vaccine Research Center - US**
  - S genetically stabilized for receptor binding conformation
  - Phase 2 testing in 18-55; 56-70, and >71-year olds
  - Phase 3 targeted for summer 2020
- **BioNTech/Pfizer/FOSUN – Germany - China**
  - RNA vaccine and a self amplifying RNA vaccine
  - Phase 1/ 2 trials in Germany and US

Limited safety information, Use lipid nanoparticles for adjuvant and delivery, Doses are easily manufactured levels of RNA

Data as of 6/30/20

DNA vectored vaccines



- **Inovio Pharmaceuticals – US and South Korea**
  - Phase 1 trial – US
  - Phase 1/ 2 trial – South Korea
  - Use electroporation for injection of DNA
  - Scaling production of electroporators

Substantial safety information. Require large amounts of DNA

Data as of 6/30/20

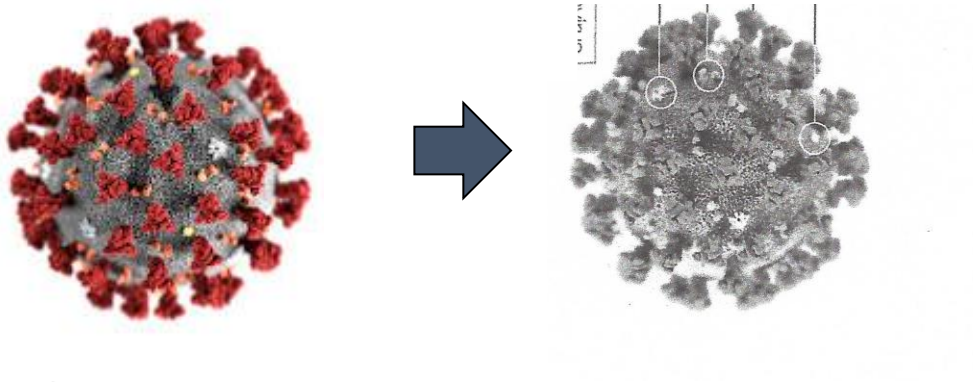
S subunit vaccine

- **Sanofi/GSK – France, England**
  - Sanofi to produce S protein
  - GSK to supply adjuvant
  - Not yet in clinical trials

Monitoring closely for immune enhancement

Data as of 6/30/20

Whole killed vaccine



- **Sinovac – China**
  - Formalin inactivated, alum adjuvant
  - Phase 3 targeted to start in July
- **Sinopharm – China**
  - Inactivated whole vaccine
  - Phase 1 / 2

Monitoring closely for immune enhancement

Data as of 6/30/20

Phase 3 testing

- **Three major efforts**
  - **Solidarity – WHO**
    - Mobile units move to local outbreaks
    - Directly comparing vaccines, a common placebo
  - **Warp Speed – US**
    - Using established vaccine trial sites plus "surge" clinics
    - Projecting 30,000 participant trials
    - Moderna RNA to be tested first, targeted to start summer 2020
  - **Chinese**
    - Conducting trials in Brazil
    - Manufacturing at Butantan Institute
    - Targeted start, summer 2020

Data as of 6/30/20

Endpoint for Success

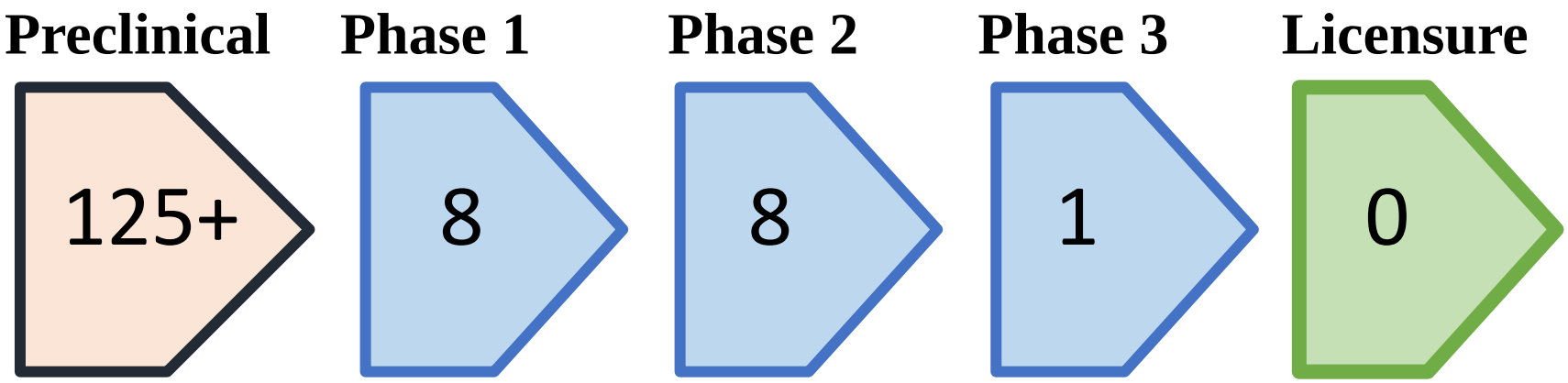
- **Number of people with confirmed infections who develop symptoms in the treated arm compared to the placebo arm.**
- **Will need to vaccinate 15,000 to 20,000 volunteers in a population that has a 1% per year incidence**
- **If the vaccine prevents COVID-19 symptoms at least 50% of the time, efficacy should be clear in 6 months - after about 150 infections**

Data as of 6/30/20

Science, 368: 1295

WHO mobile vaccine unit

Ongoing Pipeline for SARS CoV-2 vaccines



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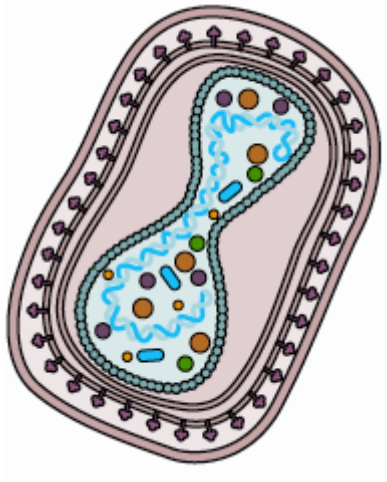
Our advancing vaccine, GeoVax Modified Vaccinia Ankara

- Pox vector has sufficient genetic space to carry genes to express SARS-CoV-2 virus like particles
- Three constructs expressing E, M, and various forms of S undergoing down selection



Attractive features of our poxvirus vectors

1. Single dose immunizations
2. MVA vector confers durability on elicited antibody
3. Pre-existing immunity limited to those vaccinated for smallpox
4. Extensive safety data

Accelerating vaccine development without compromising safety

Combining Phase 1 /2 trials

Process development and manufacture proceeding “at risk” while Phase 1-3 trials are being conducted

Planning for equitable initiation of immunizations as soon as efficacy trials are completed

When could we have a vaccine?

- **Could know if Oxford ChAd, Moderna RNA or Sinovac whole inactivated vaccines work by 2021**
- **Speed of deployment will depend on manufacture**
  - Trained personnel
  - cGMP Facilities
  - Sufficient raw materials

Rule of thumb – actual timelines are at least 2x longer than fastest possible

Goal: To add SARS-CoV-2 to viruses for which we have vaccines