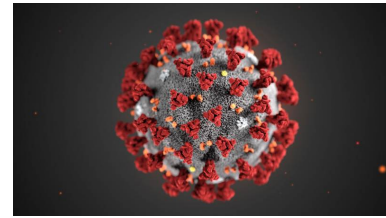


### The Virus

- COVID-19 (SARS-CoV) is one of several coronaviruses: 4 are known to cause the common cold, one was SARS (2004) and the other MERS (2012).
  - SARS is considered contained and MERS is restricted to the Arabian Peninsula; neither have a vaccine.
  - They are far less infectious but more fatal (10-50% fatality rate) than the current COVID-19.
- It's called a coronavirus because of the "crown" of protein spikes on the surface
- All coronaviruses are spread through aerosolization and mucus exposure.
- COVID-19 has been shown to last about 4 days on impermeable surfaces and about 2 days on permeable surfaces.
- The virus is a sack of fat with protein spikes on the outside and messenger RNA (mRNA) on the inside.
  - The virus itself is not alive, but the protein spikes attach to the cell it is infecting via the ACE2 (Angiotensin-Converting Enzyme 2) receptor.
  - The ACE2 receptor is a vasodilator that influences blood flow, making it a poor target for treatment or a vaccine.
  - The ACE2 receptor is found all over the body but is prevalent on lung cells lining air sacs, which is why this virus infection can cause pneumonia.
  - Once the virus attaches to the cell via the protein spike, it injects the mRNA into the cell which takes over cellular genetic reproduction, causing the cell to become a virus factory. Eventually the cell bursts and releases additional virus.
  - Mutations have been found on the structure of the protein spike which make the virus more infectious (easier to spread) but not to date more virulent (doesn't cause more or more serious disease).
  - **Genetic sequence completed 1/11/2020**



### Infectivity

- COVID-19 is 3 times more infectious than other respiratory viruses.
- The chances of being exposed depend on how many virus particles you are exposed to and the length of time you are exposed.
  - **Maximum exposure time is only 15 minutes.**
- The infection rate in the US is 15 times that of the rest of the world, and the world is going through Phase 2 – including the US. **We do not have this under control. All 50 states are experiencing spikes higher than previously seen, almost all are showing third wave spikes.**
  - **WE ARE NOW AT 1 IN 14 PEOPLE INFECTED IN THE US – IF THE SPIKES CONTINUE, WE MAY BE AT 1 IN 3 BY MARCH. LA is at 1 in 5. There are 2000-3000 deaths per day and 200,000-300,000 new infections per day. At current 88,000 new cases a day that's 1 every second**
  - Countries that had previously controlled spread are re-experiencing rising infection rates (142 countries). India and Brazil have infection rates similar to the US.
- All ages can be infected. The severity of the symptomatic response is correlated to age and the presence of other underlying medical conditions, but not exclusively.
- All ages are infectious.
  - **40% of those who are infected are asymptomatic**, but they are still infectious (they just don't know it and neither do you).

- For those who are infected and will go on to develop symptoms, **they are infectious (more highly infectious) for up to 8 days before symptoms emerge** (so again they don't yet know they are infectious and neither do you- and that could be 2 Sundays).
- A recent study of young children in the US showed that children – who are mostly asymptomatic – have up to **25 times** the amount of virus in the nasal passages than hospitalized adults. They can be significant vectors of community spread. At last count, testing has shown that 40-90% of children in spots are infected.
- Demonstrated cases of re-infection have been documented. It is not known whether the virus becomes latent (stays in the body and re-emerges, similar to chicken pox becoming shingles later in life). The re-infection appears to be a mutated version of the virus, and the second infection brings more significant symptomatology. This means the virus is endemic – it will always be with us – and that eventual vaccines may be annual.
- “exposure” is multiplicative – if you've met with 10 people during the day and they've each met with 10 people, you've been potentially exposed to 100 people

### Status

- **Currently WHO reports more than 106.5 million confirmed cases of COVID-19 globally with more than 2.4 million reported deaths**
  - 219 countries are involved
  - In the US, we have more than **27.3 million** confirmed cases and 469,000 deaths
  - A person dies from COVID every 15 seconds (average globally, World Health Organization)
- **Significant mutations have emerged (2021) – all are in the US**
  - More than 4000 identified and sequenced
  - UK mutation is highly (more) infectious, may be more virulent and fatal, and appears to be covered by the current mRNA vaccines albeit at slightly lower efficacy – doubling every 10 days in US – in more than 35 states
  - South Africa mutations also more infectious but appears to have mutated a critical part of the protein spike that makes it more refractive to mRNA vaccines, and may be more virulent; one mutation covered by existing vaccines but at reduced efficacy, one may not be covered by current vaccines ; in several states (MD VA SC)
  - Brazil mutation is more highly infectious and virulent; not completely clear that vaccines will cover it; in two states (OK MN)
  - Mutation in California is thought to be causing significant spikes there
  - Additional mutation from Brazil does not appear to be covered by vaccines

### Fatality, Co-Morbidity and Long-Term Sequelae

- COVID-19 is **10 times more fatal than the flu** (COVID-19 has an overall 1% fatality rate; the flu is about 0.1%)
- A 1% fatality rate in the US is 3.3 Million people
- Currently in the US 1 person dies about every 70 seconds from COVID; in the EU it's about 1 every 17 seconds
- **Currently more people have died in the US from coronavirus in one year than all soldiers died in WWII in 4 years combined**
- The fatality rate is generally correlated to age and underlying medical conditions
  - Fatality is 30.5/1000 for 85 years of age and above (3%)
  - Fatality is 6/1000 for 65-84, 4/1000 for 50-64, 1/900 18-29, 0.3/1000 5-17
- The virus affects the respiratory system but also the heart, liver, kidneys, GI tract, central nervous system, pancreas (causing diabetes), thyroid (affecting metabolism), and causes significant clotting in small blood vessels
- The **long-term consequences** are far more significant than other viruses: for every 1 fatality there will be:

- 19 hospitalizations (62 million)
- 18 who develop permanent heart damage (in one study, 80% of those who recovered showed heart damage by MRI) (59 million)
- 10 who develop permanent lung scarring and damage (32 million)
- 3 who develop permanent kidney damage (10 million)
- 3 strokes (10 million)
- 2 permanent neurological defects (up to and including psychoses, especially in younger population) (6.5 million)
- 2 significant cognitive dysfunctions (6.5 million)
- Long-lasting nerve damage, affecting everything from smell to walking

### **Symptoms**

- Early cardinal symptoms include loss of taste and smell, fatigue, shortness of breath, fever, dry cough, joint pain, heaviness in the chest; Progressive symptoms include acute respiratory failure, sepsis, intravascular coagulation (blood clots), and multi-organ failure
- Symptoms are long-lasting – 3 months' post recovery only about 12% are symptom-free, and symptoms can recur after abating
- Stillbirths with infection have been reported to be as high as 80% of pregnancies

### **Treatments**

- There are very few significantly effective treatments for COVID-19
- Normal flu treatments (neuraminidase and endonuclease inhibitors) do not work on COVID-19
- Early in the infection treatment with an anti-viral (Remdesivir) showed some promise; later (smaller studies) have called that into question. Remdesivir just approved by FDA for COVID (10/20); the only approved treatment
- Later in the infection, to stem a hyper-immune response and cytokine storm (causing significant inflammation in the body, the cause of some of the long-term consequences), anti-inflammatory agents (Dexamethasone, a steroid) have been shown to be marginally useful
- Convalescent plasma has also shown some promise but has not been sufficiently tested to demonstrate proof. FDA has not approved convalescent plasma for treatment.
- Some physical manipulation, such as lying the patient on their stomach instead of their back, has provided some relief of lung damage
- Studies with monoclonal antibodies for treatment and potentially prevention are underway (this approach has been shown to be effective for Ebola)
  - In November 2020, the FDA granted emergency use authorization to two monoclonal antibody treatments (bamlanivimab, made by Eli Lilly; and a combination of casirivimab and imdevimab, made by Regeneron). Both treatments have been approved for non-hospitalized adults and children over age 12 with mild to moderate COVID-19 symptoms who are at risk for developing severe COVID-19 or being hospitalized for it. In these patients, the approved treatments can reduce the risk of hospitalization and emergency room visits. These therapies must be given intravenously (by IV) soon after developing symptoms.

### **Immunity**

- The native immune response to COVID-19 has generally been shown to be weak and short-lived
- T-cell response (one of the types of normal immune cells in the body) to the virus may be a more important measure of long-duration immunity than antibody formation and duration, however, tests for antibody are quick and inexpensive, whereas testing for T-cell response is difficult and expensive
- Currently there have been antibodies demonstrated 3-4 months after infection and at least 8 months after vaccination
- Documented re-infections show that native immunity is too specific to cover mutations

### **Vaccines**

- There are currently almost 200 vaccines in various stages of testing (164 pre-clinical, 64 Phase 1, 17 Phase 2, 8 Phase 3)
- Twenty vaccine candidates are currently in Phase III (large-scale human) testing
  - Two utilize an mRNA technology, using snippets of the coronavirus mRNA that will infect but not cause disease, to prime the immune system into recognizing the virus and providing early immunity (Moderna and Pfizer)
  - both vaccines have been shown to be highly effective (95%)
  - mRNA vaccines have never been commercialized in the US and require extreme transport and storage conditions (up to -70° F), making them difficult to use and requiring some additional safety information for review and approval
  - both have been approved by FDA and the EU board of health for emergency approval and are beginning to be rolled out per CDC guidelines (approved only for ages 16 and up)
  - initial side effects are generally mild flu-like symptoms; anaphylaxis is rare but under evaluation
  - takes 2-4 weeks for immunity to develop – can still be infected during that time and can still pass the virus after immunization
  - boosters 3-4 weeks apart to get to full immunity potential
  - If you have had COVID wait 90 days before getting the vaccine to avoid competing with natural antibodies
  - These manufacturers have made all safety data available to consumers
  - These are showing results similar or better to the antibody and T-cell responses after recovery from the virus (similar to the body's response)
  - The early vaccine data shows that the vaccine appears as effective in older patients as in younger (not true for all vaccines).
  - Testing combinations of vaccine and different booster, as well as testing boosters for key mutations
- Other vaccines are using traditional vaccine manufacture processes, similar to the vaccines on the market today
  - These will be easier to manufacture/transport/store globally – no extreme refrigeration required
  - Astra-Zeneca and Janssen have completed Phase III and will soon petition FDA for EUA; AZ vaccine is approved in the UK. Emergency Use Approval for Janssen (1 shot) expected in February.
  - AZ shown to be significantly less effective than first thought esp. for 65 yoa+; trial stopped in South Africa
  - Novovax entering PhIII; early results looks good even against variants
  - These are showing results similar to the antibody and T-cell responses after recovery from the virus (similar or slightly better than the body's response)
  - Others from known US pharma companies known for vaccine development are in Phase II/III clinical trials

Platform	Attributes	Doses	Vaccine Candidate (Manufacturer)
mRNA	Fast development speed; low- to-medium manufacturing scale	2	BNT-162b2 (Pfizer, BioNTech); mRNA-1273 (Moderna)

Platform	Attributes	Doses	Vaccine Candidate (Manufacturer)
DNA	Fast development speed; medium manufacturing scale	2	INO-4800 (Inovio)
Viral vector	Medium development; high manufacturing scale	1 or 2	AZA-1222 Ad5-CoV (AstraZeneca; Oxford University); Ad26.COVS.2.S (Johnson & Johnson)
Protein subunit	Medium- to-fast development; high manufacturing scale	2	NVX-CoV2373 (Novavax)

- Many manufacturers are taking a risk and beginning to produce stockpiles of the vaccines before approval to be ready as early as possible
- Manufacturers and scientists are also engaged in an unprecedented open-source data share
- **Vaccine rollout is slower than anticipated in the US**
  - First vaccinations will go to first responders, health care workers, those at highest risk
  - The majority of the population will not likely be vaccinated before the middle of next year (June-August)
  - Current surveys show that 30% of Americans say they will NOT get the vaccine
  - **Only vaccinations will protect – simply having the vaccine and expecting others to be vaccinated will not provide epidemiologic protection sufficient to stop virus spread**

**GET YOUR FLU SHOT THIS YEAR!**

## Session Responsibilities

### Spiritual

- Session Elders are spiritual leaders of the church, so if people are feeling disconnected, part of your role is to keep in touch and make sure they know they are still beloved and in prayers. This is not just the responsibility of the pastor!
- Consider creating an Elder-in-Touch list by dividing up congregational members amongst Elders so there's always a primary contact for each person. Cards (especially with holidays coming up), calls, emails, are all great and easy ways to stay in touch.

### Administrative and Worship

- Session is responsible for the use and conditions of use for the building, and for decisions around that.
  - Because of that Session is also then responsible to monitor and enforce any conditions of use of the building you establish. This is NOT the responsibility of the pastor.
  - Whatever conditions of use you establish must be enforced both for the congregation, committees, and outside groups.
- Create a decision tree that takes into consideration the COVID status, vulnerable populations, the building itself, and vulnerability (if any) of your pastor, as well as the ability of the church to conduct virtual worship.
- Pick a CREDIBLE data source on which to base decisions (hint – Facebook isn't it).
  - In Ohio, use the Ohio government color-coded system – it's made up of 7 medically-relevant and medical system utilization data points that are objective and unbiased. Presbytery STRONGLY urges churches to meet virtually if your county is red or purple.
  - In Kentucky and Indiana, use the system at covidactnow.org - it's made up of 5 medically-relevant and medical system utilization data points that are objective and unbiased. Presbytery STRONGLY urges churches to meet virtually if your county is orange or red.
  - CDC also has a county-by-county search tool and is very credible, objective and unbiased.
- Pick ONE data source and stick to that – you will drive yourself crazy if you try to reconcile data from multiple sources, as reports are compiled at different times.
- Presbytery STRONGLY urges churches to stay virtual right now
- Presbytery STRONGLY urges churches that elect to go back to in-person worship to do the following:
  - Masks are mandatory and to be worn at all times.
    - Session members should plan to either provide masks for people who have signed up in advance (see below) and don't have one, or turn them away
    - Singing only if masked. Better to not sing at all; there are ways to have hymns played on the piano (maybe words on a screen if you have one).
    - Nothing that blows air around during worship – if your heater blows air over the congregation, pre-heat the room, turn the blower off during the service (encourage coats and sweaters if you must)
    - More than 6 feet physical distancing between family groups – estimate in advance how many people your sanctuary can realistically hold with at least 6 feet distance
    - Limit anything that is passed around or touched by multiple people.
      - Leave collection plates in the back for people to put offerings in
      - Leave communion elements in the back for them to pick up in advance or have them bring their own
    - Have a sign up sheet before the service so you can estimate how many people want to come (and cut off the sign up when you've reached your calculated maximum).
      - If people try to come in who have not signed up in advance, Session members need to be at the door to tell them no

- Have a sign up sheet before service in case you need to do contact tracing should there be an exposure
  - If there is an exposure, contact the local Board of Health immediately and shut the building and in-person meeting down for 2 weeks
  - Exclude use of bathrooms or any other part of the building (or limit bathrooms to one person at a time and provide alcohol wipes for them to clean surfaces they've touched)
- Understand your personal and church liability if someone is exposed during a church service

Vaccine	Clinical Trials	Results	Regulatory Status
<p>BNT-162b2 (2 injections) Pfizer (nucleoside-modified messenger RNA (modRNA) vaccine that encodes an optimized SARS-CoV-2 receptor-binding domain (RBD) antigen)</p>	<p>Phase 3 trial ongoing in individuals 43000+ 16 y and older, 40% diverse; 40%&gt;55yoa</p> <p>In mid-October 2020, company allowed by FDA to expand phase 3 trial to adolescents 12 y and older.</p>	<p>Primary efficacy analysis: 95% effective against clinically evident COVID-19 infection 28 d after 1st dose across all subgroups [9]</p> <p>Well tolerated across all populations [9]</p> <p>170 confirmed cases (placebo group, 162; vaccine group, 8) 10 severe cases after 1st dose (placebo group, 9; vaccine group, 1) [9]</p> <p>Efficacy consistent across age, sex, race, and ethnicity [9]</p> <p>Not evaluated for asymptomatic infection/carriage [9]</p>	<p>First approved in United Kingdom on December 2, 2020</p> <p>Approved in early December 2020 by Bahrain and Canada</p> <p><a href="#">Emergency use authorized</a> by FDA on December 11, 2020.</p>
<p>mRNA-1273 (2 injections) Moderna (encodes the S-2P antigen)</p>	<p>US phase 3 trial (COVE) ongoing 30000+, 18yr +; 40% diverse</p> <p>Phase 2/3 trial began in adolescents 12-17 y in December 2020</p>	<p>Primary efficacy analysis: Efficacy rate 94.1%</p> <p>196 confirmed cases (placebo group, 185; vaccine group, 11)</p> <p>Only severe illness (30 cases) was in placebo group, including 1 death [13]</p> <p>90 d after 2nd dose (30 participants): high levels of binding and neutralizing antibodies that fell but remained elevated</p> <p>Well tolerated [10]</p>	<p><a href="#">Emergency use authorized</a> by FDA on December 18, 2020.</p>



Vaccine	Clinical Trials	Results	Regulatory Status
<p>AZA-1222 (2 injections) AZ-Oxford (replication-deficient chimpanzee adenoviral vector vaccine containing the surface glycoprotein antigen (spike protein) gene. This vaccine primes the immune system by eliciting antibodies to attack the SARS-CoV-2 virus)</p>	<p>Phase 3 trials ongoing. One dosing regimen (n = 2741) showed vaccine efficacy of 90% when given as a half dose, followed by a full dose at least 1 month later. Another dosing regimen (n = 8895) showed 62% efficacy when given as 2 full doses at least 1 month apart. The combined analysis from both dosing regimens (N = 11,636) resulted in an average efficacy of 70.4%. All results were statistically significant (p&lt; .0001). [15] Concerns about the clinical trial implementation and data analysis have emerged because the half-dose regimen was not in the approved study design. [16, 17]</p>	<p>Participant in United Kingdom diagnosed with transverse myelitis, triggering temporary hold on trial. Interim analysis of phase 3 clinical trial in United Kingdom, Brazil, and South Africa: Efficacy 90%, depending on dosage; average efficacy of 70.4% in combined analysis of 2 dosing regimens. 131 COVID-19 cases: from 21 d after 1st dose, 10 hospitalizations, all in placebo group (2 classified as severe; 1 death)</p>	<p><a href="#">Approved in United Kingdom</a> December 29, 2020.</p> <p>Phase 3 in United States.</p>
<p>Ad26.COVS.2.S (1 injection) Janssen  adenovirus serotype 26 (Ad26) recombinant vector-based vaccine)</p>	<p>Phase 3 trial (ENSEMBLE) ongoing Second phase 3 trial (EMSEMBLE 2) announced November 15, 2020, to study effects of 2 doses</p>	<p>Phase 1/2a study: antibodies to SARS-CoV-2 observed after a single injection 99% were positive for neutralizing antibodies against SARS-CoV-2 at day 29: strong T-cell responses and a T<sub>H</sub>1 response were also noted [11]</p>	<p>Rolling biologics license application submitted in Canada and Europe on December 1, 2020.</p>

Vaccine	Clinical Trials	Results	Regulatory Status
<p>NVX-CoV2373 Novovax (recombinant nanoparticle technology from SARS-CoV-2 genetic sequence to generate an antigen derived from the coronavirus spike protein. This is combined with an adjuvant (Matrix-M). Results of preclinical studies showed that it binds efficiently with human receptors targeted by the virus)</p>	<p>Phase 3 trial in United Kingdom concluded enrollment at end of November 2020. US and Mexico phase 3 trial began December 2020.</p>	<p>Phase 1 data showed the adjuvanted vaccine induced neutralization titers in healthy volunteers that exceeded responses in convalescent serum from mostly symptomatic patients with COVID-19. <a href="#">[12]</a></p>	<p>Phase 3</p>

## Other Vaccines in Development

Vaccine	Comments
<p>INO-4800 (Inovio Pharmaceuticals) <a href="#">[19]</a></p> <p>DNA-based, 2-dose vaccine</p>	<p>Stable at room temperature for more than 1 y; frozen shipment not needed; interim results from phase 1 human trial (n = 40): favorable safety and immunogenicity; expanded to include older participants. <a href="#">[46]</a></p> <p>Phase 2/3 trial (INNOVATE) ongoing; phase 2 to evaluate 2-dose regimen (1 mg or 2 mg) vs placebo in 400 participants.</p> <p>Grant from Bill and Melinda Gates Foundation to speed testing and scale up a smart device (Celectra 3PSP) for large-scale intradermal vaccine delivery; company has also received funds from the US Department of Defense.</p>
<p>CVnCoV (CureVac) <a href="#">[20]</a></p> <p>mRNA, 2-dose vaccine</p>	<p>Preliminary data from phase 1 dose-escalating trial: 12-<math>\mu</math>g dose provided IgG antibody levels similar to convalescent plasma. phase 2b/3 trial enrollment (goal, 35,000 in Europe and Latin America) ongoing.</p>
<p>Vaccine candidates V590 and V591 (Merck) <a href="#">[21]</a></p>	<p>Vaccine V591 to be based on a modified measles virus that delivers portions of SARS-CoV-2 virus. phase 1 trial ongoing.</p> <p>Vaccine V590 uses Merck's Ebola vaccine technology; human trials ongoing.</p>
<p>COVID-19 S-Trimer (GlaxoSmithKline [GSK]) <a href="#">[22]</a></p>	<p>Partnering with multiple companies using GSK's adjuvants (compounds that enhance vaccine efficacy).</p>
<p>CpG 1018 adjuvant vaccine (Dynavax) <a href="#">[23]</a></p>	<p>Under development with Sanofi's S-protein COVID-19 antigen and GSK's adjuvant technology that stimulates the immune system; phase 1/2 trial ongoing.</p>
<p>UB-612 multipeptide-based vaccine (COVAXX [division of United Biomedical, Inc]) <a href="#">[24]</a></p>	<p>Comprises SARS-CoV-2 amino acid sequences of the receptor binding domain; further formulated with designer Th and CTL epitope peptides derived from the S2 subunit, membrane, and nucleoprotein regions of SARS-CoV-2 structural proteins for induction of memory recall, T-cell activation, and effector functions against SARS-CoV-2.</p> <p>Company partnering with University of Nebraska Medical Center in the United States; phase 1, open-label, dose escalation study ongoing in Taiwan.</p>
<p>HaloVax (Hoth Therapeutics; Voltron Therapeutics) <a href="#">[25]</a></p>	<p>Collaboration with the Vaccine and Immunotherapy Center at Massachusetts General Hospital; use of VaxCelerate self-assembling vaccine platform offers 1 fixed immune adjuvant and 1 variable immune target to allow rapid development.</p>
<p>Nanoparticle SARS-CoV-2 vaccine (Ufovax) <a href="#">[26]</a></p>	<p>Vaccine prototype development utilizing self-assembling protein nanoparticle (1c-SapNP) vaccine platform technology.</p>
<p>PDA0203 (PDS Biotechnology Corp) <a href="#">[27]</a></p>	<p>Utilizes Versamune T-cell-activating platform for vaccine development.</p>

Vaccine	Comments
CoVLP recombinant coronavirus virus-like particles (Medicago and GlaxoSmithKline) [28]	Combines Medicago's recombinant coronavirus virus-like particles (rCoVLP) with GSK's adjuvant system; phase 2/3 trial ongoing.
AS03-adjuvanted SCB-2019 (Clover Pharmaceuticals) [44]  Subunit vaccine containing SARS-CoV-2 spike (S) protein	Phase 1 trial results reported in December 2020 showed high level of antibodies. Phase 2/3 trial launching by end of 2020 using GSK adjuvant with goal of 34,000 volunteers.
Covaxin (Bharat Biotech and Ocugen) [45]  Whole-virion inactivated vaccine	Developed and manufactured in Bharat Biotech's bio-safety level 3 biocontainment facility. Co-development with Ocugen announced for the US market.  Elicited strong IgG responses against spike (S1) protein, receptor-binding domain (RBD) and the nucleocapsid (N) protein of SARS-CoV-2 along with strong cellular responses in Phase 1 and 2 clinical trials (n ~1000).  Phase 3 trial is in progress in India that involves 26,000 volunteers.
Recombinant adenovirus type-5-vectored vaccine (Ad5-vectored vaccine; Sinopharm [China]) [29]	Approved in China and Saudi Arabia; preliminary data: 86% efficacy; phase 2 trial: seroconversion of neutralizing antibodies seen in 59% and 47% of those in 2-dose groups; seroconversion of binding antibody seen in 96-97% of participants; Positive specific T-cell responses seen in 88-90% of participants.
CoronaVac (Ad5-vectored vaccine; Sinovac [China]) [47]	Limited use in China. Interim phase 3 efficacy reports vary widely from several trials. A trial in Brazil reports efficacy of 50-90%. However, a Turkish trial reports 91.25% efficacy (n = 7,371; data analysis based on 1322 participants – 752 vaccine and 570 placebo).
rAD26 (frozen) and rAd5 vector-based (lyophilized) formulations (Sputnik V; Moscow Gamaleya Institute) [30]	Phase 1/2 trial complete; approved in Russia; both vaccines safe and well tolerated with mostly mild adverse events and no serious adverse events; all participants produced anti-spike protein and neutralizing antibodies after second dose, and generated CD4+ and CD8+ responses.
hAd5 -COVID-19 (ImmunityBio) [31]	Phase 1 trial ongoing; vaccine targets inner nucleocapsid (N) and outer spike (S) protein, which have been engineered to activate T cells and antibodies against SARS-CoV-2, respectively.  These dual constructs offer the possibility for the vaccine candidate to provide durable, long-term cell-mediated immunity with potent antibody stimulation to patients against both the S and N proteins.

Vaccine	Comments
MRT5500 (Sanofi and Translate Bio) <a href="#">[32]</a>	mRNA-based vaccine candidate; preclinical evaluation demonstrated favorable ability to elicit neutralizing antibodies using a 2-dose schedule administered 3 wk apart; phase 1/2 trial anticipated to start in Q4 2020.
AG0302-COVID19 (AnGes and Brickell Biotech) <a href="#">[33]</a>	Adjuvanted DNA vaccine in phase 1/2 study in Japan; data readouts expected in Q1 2021; intent to follow with phase 3 trials in United States and South America.

#### Non-Injectable Vaccines in Development

Noninjectable Vaccine	Comments
Intranasal COVID-19 vaccine (AdCOVID; Altimune, Inc) <a href="#">[34]</a>	Single-dose vaccine; preclinical results completed at University of Alabama Birmingham showed stimulation of antigen-specific CD4+ and CD8+ T-cells in mildly affected lungs as early as 10 d; phase 1 safety and immunogenicity study expected to begin in Q4 2020.
ChAdOx1 nCov-19 inhaled (University of Oxford) <a href="#">[35]</a>	Dose-ranging trial for orally inhaled vaccine beginning phase 1 trials in 30 volunteers in Fall 2020.
saRNA inhaled (Imperial College of London) <a href="#">[35]</a>	Dose-ranging trial for orally inhaled vaccine beginning phase 1 trials in 30 volunteers in Fall 2020.
VXA-CoV2-1 oral vaccine (Vaxart) <a href="#">[36]</a>	Recombinant adenovirus vector type 5 (Ad5) expressing coronavirus antigen and a toll-like receptor 3 (TLR3) agonist as an adjuvant; theorized to confer superior protection compared with injection owing to activation of mucosal immunity; room temperature-stable vaccine tablet entering phase 1 trial in September 2020.
PittCoVacc (University of Pittsburgh School of Medicine) <a href="#">[37]</a>	Vaccine candidate using transdermal microneedle for COVID-19; testing in mice produced antibodies over a 2-wk period; microneedles are made of sugar, making it easy to mass-produce and store without refrigeration.